VOLUME 79 • NOVEMBER 1959 • NUMBER 5

A.M.A. ARCHIVES OF SURGERY

Wound Débridement
Norman W. Hoover and John C. Ivins

The Management of the Ruptured Aortic Aneurysm
John Storer and Ralph C. Smith

Radiologic Features of Isolated Ventricular Septal Defects
Edward B. Singleton, Dan G. McNamara, and Denton A. Cooley

Sarcoma of the Urachus
Donald B. Butler and Harvey S. Rosenberg

Effect of Intravenous Heparin on Terminal Temperature in the Hypothermic Dog
Leonard Caranna, Vernon Montgomery, and Henry Swan

Use of Cardiotonic Agent (Mephentermine) in Myocardial Depression Due to Potassium
Theodore Cooper, Vallee L. Willman, Panagiotis Zafiracopoulos, and C. Rollins Hanlon

Primary Idiopathic Segmental Infarction of the Greater Omentum
Earl J. Halligan and Fouad A. Rabiah

Choledochocolic Fistula
Lawrence G. Hampson and Geoffrey Lehman

Femoral Hernia in Infancy and Childhood
Ascher Lawrence Mestel, Morton G. Farber, and Irwin Chabon

Primary Neoplasms of the Small Bowel
A. C. Broders Jr., N. C. Hightower Jr., W. H. Hunt III, J. C. Stinson, R. R. White, and Henry Laurens Jr.

A Study of Uropepsin as a Reflection of Gastric Secretory Activity
James R. Jude and Alvin H. Harris

Effect of Induced Infarction on Rat Liver Implanted with Walker Carcinoma 256
Gunther E. Kraus and Arturo Beltran

The Prevention of Primary Postoperative Thrombosis
H. F. McNickle

The Roentgen Diagnosis of Mitral Stenosis
I. E. Kirsh and J. F. Kinney

The Surgical Management of Functional Adrenal Hypercorticism
Robert C. Overton, John W. Overstreet, and Ralph V. Ford

Compound Dislocation of the Knee with Popliteal Artery Injury
John G. Raffensperger and Joseph Hinkamp

Further Considerations in the Use of Hypothermia and Intermittent Cerebral Ischemia
R. W. Porter and G. J. Hayes

The Effect of Thio-TEPA on Wound Healing
Hans Rath and Irving F. Enquist

The Hyperglycemic Reaction of Alarm in Surgery
Carl O. Rice, J. H. Strickler, and Martin Beckman

Surgical Obliteration of a Coronary Artery Fistula to Right Ventricle
Henry Swan, John N. Wilson, George Woodwark, and S. Gilbert Blount Jr.

Intussusception of the Vermiform Appendix Presenting Clinically as a Cecal Carcinoma
Joe Campbell and William F. McCormick

Traumatic Pericardial Diaphragmatic Hernia
Thomas C. Moore

Reaction of the Colic Mucosa to Surgically Diverted Gastric Juice
Edwin B. Montenegro, Alvaro Dino De Almeida, Enio Vitali, and José Carlos De Rosa

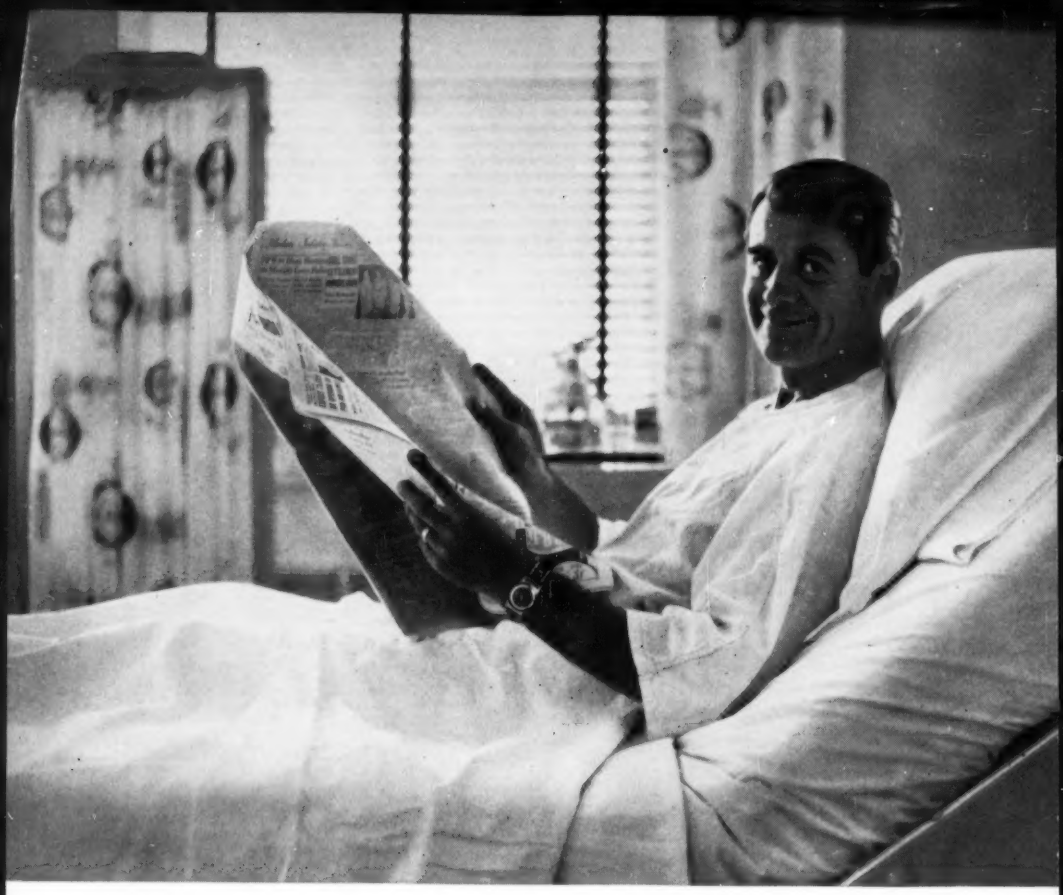
Unusual Lesions of the Appendix
Thomas J. Whelan Jr. and Max F. Rast

Segmental Motor Paralysis
Thomas F. Meaney and Charles R. Hughes

Cholecystectomy and Operative Cholangiography
Joel W. Baker and John H. Walker

Operative Cholangiography
Deward O. Ferris and John R. Hodgson

AMERICAN MEDICAL ASSOCIATION PUBLICATION



Lessened postoperative vomiting with

MORNIDINE™

- **Low dosage**
- **Selective action on the medullary chemoreceptor trigger zone**
- **Well tolerated—low incidence of side effects**
- **Parenteral and tablet forms**

Mornidine (brand of pipamazine), a product of Searle Research, offers distinct advantages in the treatment of postoperative nausea and vomiting. Its low dosage and selective action on the trigger zone combine exceptional therapeutic effectiveness with a high degree of safety and a low incidence of side effects.

Mornidine helps prevent sudden and restless emergence from general anesthesia. When given with an analgesic, the effective dose of the latter can often be diminished.

Used prophylactically or therapeutically, Mornidine offers the additional advantage of two dosage forms: tablets and ampuls for parenteral administration.

The usual adult dose is 5 mg. (1 cc.) intramuscularly or orally every 4 to 6 hours as needed.

G. D. SEARLE & CO.

Research in the Service of Medicine

CHICAGO 80, ILLINOIS

TABLE OF CONTENTS

VOLUME 79 NOVEMBER 1959 NUMBER 5

ORIGINAL ARTICLES

PAGE

Wound Débridement
Norman W. Hoover, M.D., and John C. Ivins, M.D., Rochester, Minn. 701

The Management of the Ruptured Aortic Aneurysm
John Storer, M.D., and Ralph C. Smith, M.D., Cleveland 711

Radiologic Features of Isolated Ventricular Septal Defects
Edward B. Singleton, M.D.; Dan G. McNamara, M.D., and Denton A. Cooley, M.D., Houston, Texas 715

Sarcoma of the Urachus
Donald B. Butler, M.D., and Harvey S. Rosenberg, M.D., Houston, Texas 724

Effect of Intravenous Heparin on Terminal Temperature in the Hypothermic Dog
Leonard Caranna, M.S.; Vernon Montgomery, M.D., Ph.D., and Henry Swan, M.D., D.Sc., Denver 729

Use of Cardiotonic Agent (Mephentermine) in Myocardial Depression Due to Potassium
Theodore Cooper, M.D., Ph.D., Bethesda, Md.; Vallee L. Willman, M.D.; Panagiotis Zafiracopoulos, M.D., and C. Rollins Hanlon, M.D., St. Louis 734

Primary Idiopathic Segmental Infarction of the Greater Omentum
Earl J. Halligan, M.D., Jersey City, N.J., and Fouad A. Rabiah, M.D., Highland Park, Mich. 738

Choledochocolic Fistula
Lawrence G. Hampson, M.D., F.R.C.S. (C), and Geoffrey Lehman, M.D., Montreal, Canada 746

Femoral Hernia in Infancy and Childhood
Ascher Lawrence Mestel, M.D., M.S. (Surg.); Morton G. Farber, M.D., and Irwin Chabon, M.D., Brooklyn 750

Primary Neoplasms of the Small Bowel
A. C. Broders Jr., M.D.; N. C. Hightower Jr., M.D.; W. H. Hunt III, M.D.; J. C. Stinson, M.D.; R. R. White, M.D., and Henry Laurens Jr., M.D., Temple, Texas 753

A Study of Uropepsin as a Reflection of Gastric Secretory Activity
James R. Jude, M.D., and Alvin H. Harris, M.D., Bethesda, Md. 761

Effect of Induced Infarction on Rat Liver Implanted with Walker Carcinoma 256
Gunther E. Kraus, D.V.S., and Arturo Beltran, M.D., Buffalo 769

The Prevention of Primary Postoperative Thrombosis
H. F. McNickle, F.R.C.S. (Eng.), Auckland, New Zealand 775

The Roentgen Diagnosis of Mitral Stenosis
I. E. Kirsh, M.D., and J. F. Kinney, M.D., Hines, Ill. 785

The Surgical Management of Functional Adrenal Hypercorticism
Robert C. Overton, M.D.; John W. Overstreet, M.D., and Ralph V. Ford, M.D., Houston, Texas 791

Compound Dislocation of the Knee with Popliteal Artery Injury
John G. Raffensperger, M.D., and Joseph Hinkamp, M.D., Chicago 799

Further Considerations in the Use of Hypothermia and Intermittent Cerebral Ischemia
R. W. Porter, M.D., Ph.D., Long Beach, Calif., and Lieut. Col. G. J. Hayes (MC), U.S. Army 801

The Effect of Thio-TEPA on Wound Healing
Hans Rath, M.D., and Irving F. Enquist, M.D., Brooklyn 812

The Hyperglycemic Reaction of Alarm in Surgery
Carl O. Rice, M.D., Ph.D.; J. H. Strickler, M.D., M.S., Minneapolis, and Martin Beckman, Ph.D., New Haven, Conn. 815

Surgical Obliteration of a Coronary Artery Fistula to Right Ventricle
Henry Swan, M.D.; John N. Wilson, M.D.; George Woodwark, M.B., and S. Gilbert Blount Jr., M.D., Denver 820

Intussusception of the Vermiform Appendix Presenting Clinically as a Cecal Carcinoma
Joe Campbell, M.D., and William F. McCormick, M.D., Memphis, Tenn. 825

Traumatic Pericardial Diaphragmatic Hernia
Thomas C. Moore, M.D., Indianapolis 827

Reaction of the Colic Mucosa to Surgically Diverted Gastric Juice
Edwin B. Montenegro, M.D.; Alvaro Dino De Almeida, M.D.; Enio Vitali, and José Carlos De Rosa, São Paulo, Brazil 831

Unusual Lesions of the Appendix
Lieut. Col. Thomas J. Whelan Jr. (MC), U.S. Army, and Capt. Max F. Rast (MC), U.S. Army (Res.) 838

Segmental Motor Paralysis
Thomas F. Meaney, M.D., and Charles R. Hughes, M.D., Cleveland 847

PICTORIAL FILM REVIEWS

Cholecystectomy and Operative Cholangiography
Joel W. Baker, M.D., and John H. Walker, M.D., Seattle 853

Operative Cholangiography
Deward O. Ferris, M.D., and John R. Hodgson, M.D., Rochester, Minn. 857

A. M. A.
ARCHIVES OF SURGERY

Also the Official Publication of the Central Surgical Association and the Western Surgical Association

VOLUME 79 NOVEMBER 1959 NUMBER 5

COPYRIGHT, 1959, BY THE AMERICAN MEDICAL ASSOCIATION

Published under the Auspices of the Board of Trustees

EDITORIAL BOARD

WALTMAN WALTERS, Chief Editor, Rochester, Minn.

J. GARROTT ALLEN, Chicago
ALFRED BLALOCK, Baltimore
FRANK HINMAN JR., San Francisco
G. E. LINDSKOG, New Haven, Conn.
WALTER MADDOCK, Chicago
ALTON OCHSNER, New Orleans
HENRY KING RANSOM, Ann Arbor, Mich.
RICHARD WARREN, Boston
BARNES WOODHALL, Durham, N. C.

JOHN H. TALBOTT, Editor, A.M.A. Scientific Publications
GILBERT S. COOPER, Managing Editor, Specialty Journals
T. F. RICH, Assistant Managing Editor, Specialty Journals

The A. M. A. Archives of Surgery is published monthly by the American Medical Association and is an official publication of the Association.

Executive Vice President: F. J. L. BLASINGAME, M.D.
Business Manager: RUSSELL H. CLARK

ADVERTISING: Advertising Manager, John L. Murphy; Advertising Production Manager, Walter H. Kimotek. Advertising Representatives: Vernon J. Wendt, 535 North Dearborn Street, Chicago 10, Illinois, WHitehall 4-1500; Al Detwiller, 475 Fifth Avenue—Room 1005, New York 17, New York, ORegon 9-9383; Dale B. Clarke, 1919 Wilshire Blvd., Los Angeles 57, California, HUbbard 3-3811.

CIRCULATION: Circulation Manager, Robert A. Enlow; Assistant Circulation Manager, Bernard F. Kroeger. The yearly subscription rate of the Archives of Surgery is: U. S. and Possessions, $14.00; Canada, $14.50. Other Foreign Countries, $15.50. Special price to Students, Interns, and Residents in U. S. and Possessions $8.00. Single copies of this and previous calendar year $1.50.

Back issues older that two years are available through Walter J. Johnson, Inc., 111 Fifth Avenue, New York 3, New York. Reprints of back issues available through Johnson Reprint Corporation, 111 Fifth Avenue, New York 3, New York.

CHANGE OF ADDRESS: Please notify publisher at least six weeks in advance, including both old and new address, and a mailing label taken from the most recent copy. Include your new Postal Zone number, if you live in a zoned city.

Second-class postage paid in Nashville, Tennessee.

Please address communications and subscription orders to: American Medical Association, 535 North Dearborn Street, Chicago 10, Illinois.

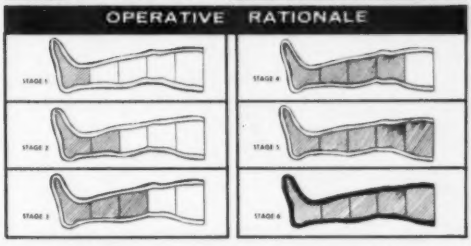
A dynamic adjunct in the treatment of edema of the extremities

THE CIRCULATOR

Completely Portable
weight only 43 pounds

Lymphedematous arm under treatment

Venous insufficiency of the leg under treatment



The semi-diagramatic pictures demonstrate the rationale involved. Once pressure is established in one segment, this pressure plus the succeeding pressures in all the segments are held until the cycle is completed, thereby effecting a 'milking' action to the extremity. The unit is designed so the more distal portions of the sleeve or boot are always under slightly greater pressure than the more proximal sections. This effectively prevents regurgitation or retrograde flow of fluid.

. . . an amazingly flexible

therapeutic unit

for the field of
PHYSICAL MEDICINE AND REHABILITATION

offering a means of actively forcing fluid from edematous extremities.

The CIRCULATOR is automatic in continuous operation, yet under complete control of the attending physician or therapist. Its unique action forces fluid from the arm or leg—by progressive cumulative pneumatic pressure in a proximal direction—toward the heart. In cases of lymphedema or venous stasis, the 'cumulative' compression effects a restoration of the return flow of blood or lymph, past the incompetent and inadequate valves of the venous or lymphatic systems.

Patients of all ages have been treated, with special emphasis on post-mastectomy lymphedema of the arm, stasis ulcer (of long duration) of the legs, lymphedemas of the praecox variety, and the post-surgical edemas of the extremities. In cases of post-mastectomy 'brawny' arm, treatment with the CIRCULATOR has resulted in marked softening of the induration, reduction or complete elimination of 'pitting', and—diminution of any attendant pain. Arms which were almost useless because of limitation of motion due to the pain of lymphedematous pressure, were dramatically restored to various degrees of usefulness. If CIRCULATOR treatment is instituted immediately upon recognition of lymphedema symptoms, the unfortunate sequelae of this distressing situation may be attenuated if not eliminated entirely.

Where incompetent circulation has caused fluid retention in dependent extremities, the CIRCULATOR will effectively displace lymph and venous blood toward the heart, thereby controlling the tendency toward lymphatic stasis with its resultant fibrotic sequelae.

In operation, the CIRCULATOR is simplicity itself. The pressure dial of the unit is set (in millimeters of mercury) to approximately 10 millimeters below the diastolic blood pressure of the extremity. No further adjustment to the machine or therapeutic casings is needed at any time. The arm or leg is slipped into the casing, and the switch turned on. Therapy is then underway. There is no discomfort to the patient, and treatment may be administered during the time of day when relaxation is in order, while watching television, reading, or just resting.

Send for this valuable folder today

CIRCULATOR THERAPEUTICS
235 West Merrick Road, Freeport, N. Y.

Please send me the new, informative folder "The Mechanical Control of Lymphedema".

Name .....

Address .....

City ..... Zone .....

State .....

5/

Instructions to Contributors

Articles, book reviews, and other materials for publication should be addressed to the Chief Editor. Articles are accepted for publication on condition that they are contributed solely to this journal.

An original typescript of an article, with one carbon copy, should be provided; it must be double or triple spaced on one side of a standard size page, with at least a 1-inch margin at each edge. Another carbon copy should be retained by the author.

The main title of an article may not contain more than eighty characters and spaces; a subtitle may be of any length.

The author's name should be accompanied by the highest earned academic or medical degree which he holds. If academic connections are given for one author of an article, such connections must be given for all other authors of the article who have such connections.

If it is necessary to publish a recognizable photograph of a person, the author should notify the publisher that permission to publish has been obtained from the subject himself if an adult, or from the parents or guardian if a child. An illustration that has been published in another publication should be accompanied by a statement that permission for reproduction has been obtained from the author and the original publisher.

Oversized original illustrations should be photographed and a print on glossy paper submitted. Prints of a bluish tinge should be avoided. Large photomicrograph prints will be reduced in scale unless portions to be cropped are indicated by the author. The author should submit duplicate prints of roentgenograms and photomicrographs with the essential parts that are to be emphasized circled, as a guide to the photoengraver.

Charts and drawings should be in black ink on hard, white paper. Lettering should be large enough, uniform, and sharp enough to permit necessary reduction. Glossy prints of x-rays are requested. Paper clips should not be used on prints, since their mark shows in reproduction, as does writing on the back of prints with hard lead pencil or stiff pen. Labels should be prepared and pasted to the back of each illustration showing its number, the author's name, and an abbreviated title of the article, and plainly indicating the top. Charts and illustrations must have descriptive legends, grouped on a separate sheet. Tables must have captions. ILLUSTRATIONS SHOULD BE UNMOUNTED.

References to the literature should be limited to those used by the author in preparation of the article. They should be typed on a special page at the end of the manuscript. The citation should include, in the order given, name of author, title of article (with subtitle), name of periodical, with volume, page, month—day of month if weekly or biweekly—and year. References to books must contain, in the order given, name of author, title of book, city of publication, name of publisher, and year of publication.

AMERICAN MEDICAL ASSOCIATION

535 North Dearborn Street **Chicago 10**

VERSATILE FURACIN

effective by intrapleural instillation[1]

the situation: Four-month-old infant with staphylococcal pneumonia and empyema resistant to most antibiotics was allergic to antibiotic chosen after sensitivity tests. Thoracentesis produced 30-40 cc. of creamy, purulent fluid. Organism was Staphylococcus aureus, coagulase positive.

then Furacin was instilled: 0.2% Solution was diluted equally with physiologic saline and 10 cc. of mixture instilled twice daily into pleural space, with suction catheter clamped off for 1 hour. Fluid almost immediately became thinner and less viscous. Twenty-four hours later infant was less irritable, voluntarily started taking food. Instillations stopped. FURADANTIN® (brand of nitrofurantoin) Oral Suspension prescribed. Recovery uneventful.

1. Perkins, J. L.: Kansas State M. J. (to be published).

FURACIN®

brand of nitrofurazone

FURACIN has been in clinical use for more than 13 years. Today it is one of the most widely prescribed single topical antibacterial agents. Like other nitrofurans, FURACIN remains effective, even in pus, sera or exudates, against pathogens which have developed—or are prone to develop—resistance to antibiotics.

FURACIN, in a water-miscible base of polyethylene glycols, is available in a number of dosage forms. Included are Soluble Dressing, Soluble Powder, Solution and Cream. Also in Vaginal Suppositories, Inserts, and in special formulations for eye, ear and nose.

NITROFURANS—a unique class of antimicrobials—neither antibiotics nor sulfonamides

EATON LABORATORIES, NORWICH, NEW YORK

10 SPECIALTY JOURNALS

PUBLISHED MONTHLY
BY THE AMERICAN MEDICAL ASSOCIATION

NEUROLOGY

GENERAL PSYCHIATRY

SURGERY

PATHOLOGY

DISEASES OF CHILDREN

OPHTHALMOLOGY

INDUSTRIAL HEALTH

DERMATOLOGY

INTERNAL MEDICINE

OTOLARYNGOLOGY

Each journal offers the latest medical research and developments of outstanding specialists. Edited for the doctor by prominent authorities in each special field, these journals are of value not only to the specialist but to the general practitioner as well.

To order your subscription to one of the A.M.A.'s specialty journals use the form below.

AMERICAN MEDICAL ASSOCIATION
535 North Dearborn • Chicago 10

Please enter my subscription to the specialty journal checked at right.
Remittance for ☐ one year ☐ two years is enclosed.

NAME_____

ADDRESS_____

CITY_____ ZONE____ STATE_____

(One year rates)	U.S.A. & Possessions APO's	Canada	Outside U.S.A. & Possessions
☐ A.M.A. Arch. Neurology	$14.00	$14.50	$15.50
☐ A.M.A. Arch. Gen. Psychiatry .	$14.00	$14.50	$15.50
☐ A.M.A. Arch. Dermatology....	12.00	12.50	13.50
☐ A.M.A. Arch. Industrial Health.	10.00	10.50	11.50
☐ A.M.A. Arch. Internal Medicine	10.00	10.50	11.50
☐ A.M.A. Jrl. Diseases of Children	12.00	12.50	13.50
☐ A.M.A. Arch. Surgery	14.00	14.50	15.50
☐ A.M.A. Arch. Pathology	10.00	10.50	11.50
☐ A.M.A. Arch. Ophthalmology..	12.00	12.50	13.50
☐ A.M.A. Arch. Otolaryngology..	14.00	14.50	15.50

It's All New!

PERIPHERAL FACIAL PALSY

By

KARSTEN KETTEL, M.A.

Head, Department of Otolaryngology

Frederiksborg County Central Hospital

Hillerod, Denmark

Surgeons the world over will welcome Doctor Kettel's fascinating account of his **vast experience** in this comparatively **new and highly specialized** field. He is the first to guide the inquiring reader through the literature with the **causes** and **treatment** of facial palsy.

Facial paralysis is serious, not because it endangers life, but because the person afflicted loses "the language of facial expression." The resulting handicap is tragic. Since 1939 Doctor Kettel has operated on **311 patients** according to the method of Bunnell, Ballance, and Duel. He is one of a very few surgeons **qualified to write on the subject** and has gained world-wide fame as a lecturer in great universities and clinics all over the world. His present study deals exclusively with cases of peripheral facial palsy in which surgical intervention was needed, suggested, and technically practicable.

PURPOSE:

- *To establish indications for surgical intervention upon the facial nerve*
- *To present results of direct nerve repair based on re-examination of patients*
- *To stress such points as are important from clinical and surgical views in improving results*
- *To describe what is actually seen at operation*
- *To discuss the significance of findings in relation to etiology and pathogenesis of peripheral facial palsy*

Well-known facts regarding normal anatomy, symptomatology, and diagnosis are mentioned only to the extent necessary for the understanding of the problem.

"Dr. Kettel has made a great contribution to our knowledge of facial palsy and it is my belief that his monograph will soon be found on the bookshelf of everyone who is interested in the subject."—*From the Foreword by TERENCE CAWTHORNE, F.R.C.S., London, England*

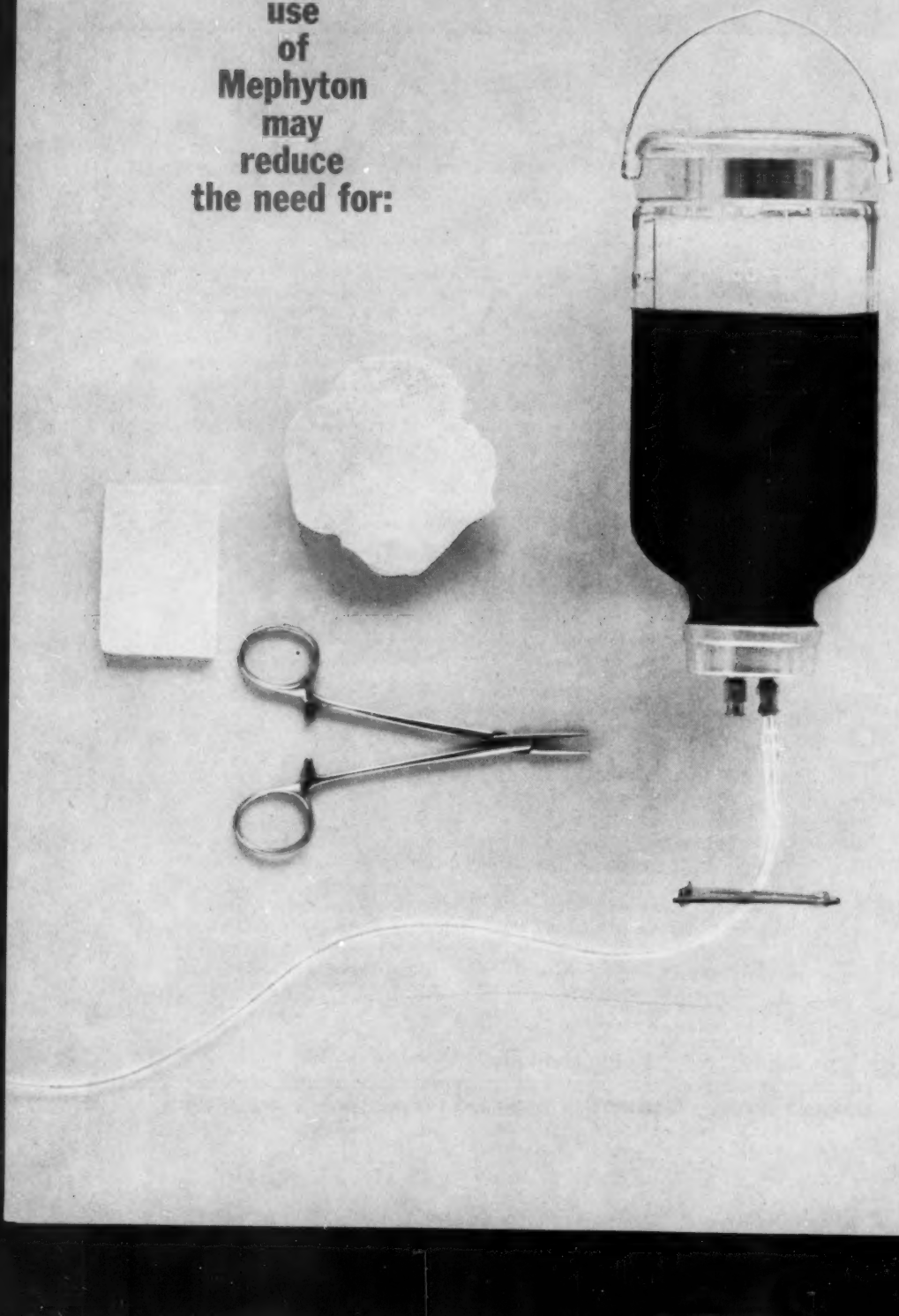
342 pp. (7x10) **$19.50**
300 il. (12 four-color plates)

Publication date October 1959

CHARLES C THOMAS • PUBLISHER • 301-327 East Lawrence Avenue • SPRINGFIELD • ILLINOIS

9/

preoperative use of Mephyton may reduce the need for:



reduce the hazard of hemorrhage due to hypoprothrombinemia

Mephyton®

Vitamin K_1

"has a more prompt, more potent and more prolonged effect than the vitamin K analogues"*

Preoperative use of 'Mephyton' reduces the likelihood and seriousness of surgical hemorrhage due to hypoprothrombinemia. 'Mephyton' is widely used before tonsillectomy, intestinal surgery, biliary tract surgery, rhinoplasty, surgery of the newborn (especially prematures), neurosurgery, thoracic surgery, obstetrical and gynecological procedures, surgery in any highly vascular area. It is particularly indicated in patients with obstructive jaundice, or when prothrombin level is depressed following administration of anticoagulants, barbiturates, salicylates, antibiotics, sulfonamides, or phenylbutazone.

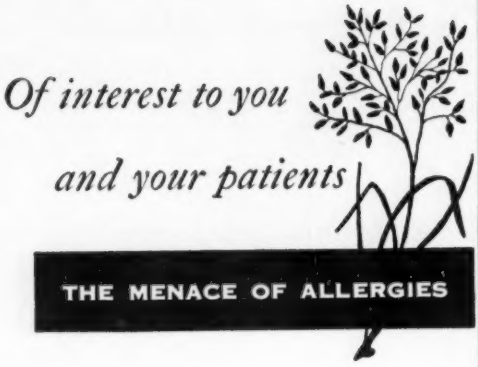
Dosage: Preoperatively, up to 50 mg. orally at least 24 hours before surgery, or up to 50 mg. intravenously at least 12 hours before surgery, to help restore prothrombin to safer levels. Postoperatively, up to 50 mg. may be given orally or intravenously after surgery to combat hemorrhage due to hypoprothrombinemia. In all situations, individual dosage requirements should be determined by prothrombin-time response.

Supplied: Tablets, 5 mg.; bottles of 100. Emulsion, 10 and 50 mg. per 1-cc. ampuls; boxes of 6.

*Council on Drugs: New and Nonofficial Drugs, Philadelphia, J. B. Lippincott Co., 1958, p. 620.

MEPHYTON is a trademark of Merck & Co., Inc.

MERCK SHARP & DOHME, DIVISION OF MERCK & CO., INC., PHILADELPHIA 1, PA.

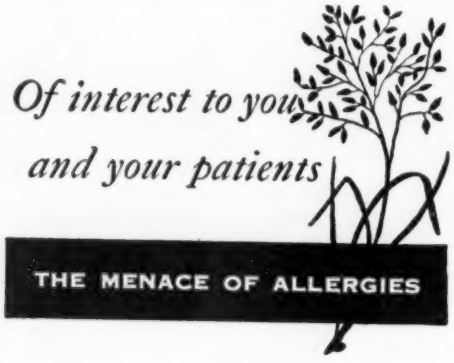


FOOD ALLERGY
by Samuel M. Feinberg, M.D., 6 pages, 10 cents

SKIN ALLERGY
by Samuel M. Feinberg, M.D., 6 pages, 10 cents

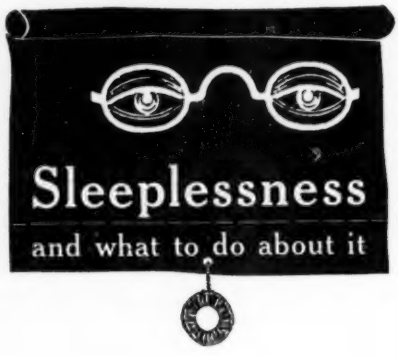
ASTHMA AND HAY FEVER
by Samuel M. Feinberg, M.D., 6 pages, 10 cents

AMERICAN MEDICAL ASSOCIATION
535 NORTH DEARBORN STREET • CHICAGO 10 • ILLINOIS



HOUSE DUST ALLERGY
by Karl D. Figley, 8 pages, 15 cents
FOOD ALLERGY
by Samuel M. Feinberg, M.D., 6 pages, 10 cents
SKIN ALLERGY
by Samuel M. Feinberg, M.D., 6 pages, 10 cents
ASTHMA AND HAY FEVER
by Samuel M. Feinberg, M.D., 6 pages, 10 cents
RAGWEED AND HAY FEVER
by Oren C. Durham, 2 pages, 5 cents

AMERICAN MEDICAL ASSOCIATION
535 North Dearborn Street • Chicago 10 • Illinois



SLEEPLESSNESS AND WHAT TO DO ABOUT IT by Donald A. Laird, Ph.D.
8 pages, 15 cents

ROADS TO RELAXATION
by Joseph L. Fetterman, M.D.
4 pages, 10 cents

AMERICAN MEDICAL ASSOCIATION
535 N. Dearborn St., Chicago 10, Illinois

A.M.A. ARCHIVES OF
SURGERY

Wound Debridement

NORMAN W. HOOVER, M.D., and JOHN C. IVINS, M.D., Rochester, Minn.

Much work must be done to prepare our population against the ravages of possible enemy attack so that national survival may be ensured. The "mass casualty" doctrine properly assumes, for planning purposes, that the casualty load will be overwhelming and that it cannot be managed by available medical manpower alone. It seems certain that our survival may depend largely on the individual citizen's ability to render effective first aid and support to himself, his family, and his neighbors. Members of the medical profession, with the help of allied paramedical professional groups, must, however, provide the leadership both in training the populace and in actually performing the task at hand. Initially, at least, specialization will cease to exist and all doctors of medicine (and others as well) of necessity will become traumatic surgeons. Here again, good training is prerequisite to success, and good training begins with fundamentals.

With these thoughts in mind, it seems advisable to consider, in some detail, the most basic issues in the care of the traumatic wound, namely wound débridement and the principles of wound healing.

Definition

The word "débridement" has been used rather superficially in reference to surgery of wounds. It is appropriate, therefore, to review what the word denotes. The term was introduced into the literature by Paré, but Desault [1] and Larrey [2] brought it into wide favor. The metaphorical import of the word alluded to the unbridling of a horse, and implied simple incision of wounds to provide drainage and to relieve pressure. Débridement was first used in its anglicized sense during the First World War by Depage [3] of Belgium, and the connotation of "débridement" in the sense of "wound excision" gained common usage in the literature of that time. Between wars, the word was used loosely to mean any early surgical treatment of wounds. In the early 1940's, after an exercise in dialectic, the etymologic purists were forced to concede to the pressure of common usage. Although the term "débridement" may be inexact in describing the process to which it refers, for want of an English equivalent retention of the word in the language may be justified on the grounds of economy of expression. It is now accepted that "débridement" means removal of all foreign material plus aseptic excision of all contaminated and devitalized tissue from traumatic wounds.

History

Progress in surgery has been intimately associated with war. Historically, this type of progress has resulted from the surgeon's position as "externist," dealing primarily with lesions caused by external violence. A

Submitted for publication June 1, 1959.

Fellow in Orthopedic Surgery, Mayo Foundation (Dr. Hoover); Section of Orthopedic Surgery, Mayo Clinic and Mayo Foundation (Dr. Ivins). The Mayo Foundation, Rochester, Minn., is a part of the Graduate School of the University of Minnesota.

second reason for the relationship can be found in the necessity of returning, in the unfavorable circumstances of war, to basic surgical principles and sound methods of treatment. An unfortunate consequence of the age of mechanization is that peacetime pursuits are now little less destructive than is war. Although compromise may be somewhat mitigated by the controlled environment of peacetime care, there can be no reasonable division of principle between the military treatment and the civilian treatment of wounds.

Learning by immediate and often bitter experience is seemingly a prerogative of man. When each major war breaks out, much is painfully learned, only to be forgotten and relearned by another generation in another war. A review of the history of traumatic surgery will contribute to our understanding of the principles which have evolved.

Hippocrates, and later Galen, perpetuated the even-then ancient method of the treatment of wounds by fire. Cautery of wounds was destined to persist until the 15th century. Galen also fostered the notion that suppuration was essential to the healing process. His authority was such that the favorable regard for suppuration was not successfully challenged for nearly 14 centuries.

Although its influence was insufficient to alter the accepted form of treatment, the school at Salerno, in the south of Italy, founded in the 10th century, must be granted primacy in the understanding of wound healing. This was a time of intellectual awakening, when in the search for truth men challenged the inviolability of tradition and authority. Such men were Hugo de Lucca and his son, Theodoric. They taught that healing per primum was not only possible, but desirable.[4] Theodoric wrote, "In the treatment of a simple wound—the objective is a simple one: The reunion of severed parts. . . . In the first place the lips of the wound and all about the wound should be debrided (abradantur); and then the wound should be completely cleansed of fuzz, hair and anything else, and let it be wiped quite dry with fine lint soaked in warm wine and wrung out. Thus the lips of the wound may be reunited as well as possible in accordance with the original healthy state. . . ." He further wrote, "If at the beginning you have not made a suture, and if the wound should already have been altered by air, then let the sides be refreshened with some instrument, and let them be made bloody so that they may be better joined together, and then let it be sewed up and treated with incarnative medicine."[5] Débridement and secondary closure of wounds are not inventions of the 20th century.

Unfortunately, Guy de Chauliac, of Galenist conviction, was a man of greater persuasive power. He spent much time and ingenuity in the development of pus-producing potions, some "miraculously" effective. His influence was such on the continent that it overshadowed the earlier work at Salerno, and pus regained its laudability for another 500 years.

It was not until the 16th century that the doctrine of healing without interference was again expounded by Paré. The advent of gunpowder to the scene of war increased the dependence upon cautery, since it was inferred from the incidence of complications that the wounds were poisoned. By this time, the technical refinement of boiling oil had supplanted the hot iron. The Italian, Botello,[6] and Paré concurrently demonstrated the similarity of gunshot wounds to other wounds, and disproved the notion that gunshot wounds were inherently toxic. Paré's observations were occasioned by a fortuitous shortage of oil. He was forced, for want of it, to forego treatment with boiling oil for many of his casualties, who, to his surprise, fared better without it than those who were cauterized. With Paré a new epoch in surgery began.

As was noted, débridement began, nominally, with Desault. His technique of wide incision for the drainage of wounds was

generally accepted, and it led to almost immediate improvement in the results of treatment during the French Revolution. He later extended his form of treatment to include débridement as we now understand the term, meaning wound excision. Under his influence, Baron Larrey introduced wound excision as a standard operating procedure during the Napoleonic wars.

The treatment of wounds was advanced almost to modern status during the Crimean War by the brilliant Russian, Nicolai Ivanovitch Pirogoff.[7] Conversely, the management of wounds in the American Civil War was crude and badly neglected.

Only a few years later the introduction of the antiseptic technique by Lister in 1867 altered the whole concept of surgery. This technique proved not to be an unmixed blessing. Although it was not Lister's intention, his work was interpreted to imply that surgical techniques in the treatment of wounds could be supplanted by the generous use of carbolic acid. Topical antisepsis of wounds has enjoyed periodic favor ever since, perhaps the most striking example being the Carrell-Dakin chlorine compounds of the First World War.[8] The urge to kill germs ignores the fact that any substance which is bactericidal also must be cytotoxic. Hewlett calls this the "insult to injury" approach.[9]

In 1898 the German bacteriologist-surgeon Paul Friedrich documented experimental support for the technique of wound excision which he later, in 1915, established as standard operating procedure for the German First Army Corps. His concise statement of the rationale of wound excision bears reading: "1. Every non-operative contused wound infection that is so-called spontaneous wound infection, is first a local process. For therapeutic and prognostic purposes, it is important to reckon that in by far the greatest number of cases it remains so for at least six hours. . . . This time interval must certainly represent the incubation period of infection material (time of latency of infection, incubation time). 2. Of the procedures undertaken within this time allotment, precise excision (anfrischung) of the infected area into the healthy tissue, and extension of the traumatized region are the most reliable means of securing uninfected healing." [10]

Introduction of the technique of wound excision into the Allied services by Gray [11] of the British Expeditionary Forces, and Depage [3] of Belgium, during 1917 and 1918, tremendously improved our survival rates. However, because of lack of experience with the method, excision of wounds at first was immoderate, and the practice of excision and primary closure, as advocated by Gray, in less experienced hands exacted a heavy price in gas gangrene and sepsis.[12] Later reports give evidence that by the end of the war, the technique had assumed its present form.[13]

When the Second World War broke out, another generation of surgeons, schooled in the less exacting art of civilian practice, with almost complete ignorance of the well-documented experience of World War I, or of the more recently published experience of Koch,[14] of Orr,[15] and of Trueta [16,17] in the Spanish Civil War, had to relearn these same lessons. By this time, antibiotic and chemotherapeutic agents had exerted their influence for both good and evil. After the promising reports obtained from the use of sulfonamide compounds among the wounded at Pearl Harbor, optimists were again lulled to compromise with principles, again with unpleasant consequences. In the foreseeable future we will have no substitute for careful adequate surgical débridement.

The fact that these experiences are recent seems not to have altered the pattern. Again in Korea, general unfamiliarity with the principles of débridement was demonstrated by the increased morbidity and mortality rates coincident with the arrival of each new group of military medical officers.[18]

Physiology of Wound Healing

Prerequisite to intelligent management of wounds is an understanding of the biologic

consequences of trauma and of the natural mechanisms of repair. The healing of a wound begins at the time of injury, with the exudative phase. The purpose of this period is elimination of material incompatible with incorporation, the establishment of adequate defenses, and preparation for definitive repair. This is initiated by a vascular response. Capillary permeability is increased by trauma, anoxia, stasis, and bacterial toxins, with a resultant perfusion of blood and transudate.[19] The release of a leukotactic substance by injured tissue and bacterial cells promotes the movement of polymorphonuclear leukocytes into the area, where they in turn liberate proteolytic enzymes, and with histiocytes and macrophages share the function of phagocytosis.

Lagging somewhat behind, and reaching a peak only after four to five days, the local and general immunologic response to exogenous bacterial protein occurs. During the exudative phase, all material incapable of survival is removed by enzymatic digestion, bacterial decomposition, or phagocytosis. The natural process of separation is inefficient and prolonged in the removal of fascia, tendons, and bone. Surgical removal of all nonviable material will greatly expedite the process of separation, and the success of surgical removal will depend upon the completeness with which it is done. This stage of healing obviously will be prolonged by rough handling of tissues, mass ligature, incomplete hemostasis, and drying of tissues. If properly managed, the healing process will assume an orderly sequence from this point.

The second stage of healing, that of reparation and proliferation, will begin on about the fifth day, if infection has been avoided. This stage begins with proliferation of granulation tissue, during which time "normal healthy granulation tissue" covers the wound, serving as an effective barrier to bacterial invasion for the rest of the healing period. The wound is progressively reduced in size by fibrosis and granulation contracture, thereby hastening the stage of epithelization.

Finally, there follows the period of contracture of scar tissue, or cicatrization. If the wound is left to heal spontaneously, this sequence will proceed slowly and safely, but often to functional and cosmetic disadvantage.

It is a lack of understanding of these time relationships which has prejudiced previous efforts at early closure of wounds. This sequence offers theoretic credence to clinical experience with delayed primary suture. It has been found that primary closure or delayed closure earlier than the fourth day, as practiced during World War I, failed with discouraging regularity. Such failure probably is explained, at least in part, by lack of understanding of the lag of several days in the establishment of immunologic defenses, as well as retention of unrecognized necrotic material. Undue delay beyond this time again prejudices closure, since, as we shall see, as granulation and fibrosis progress, the wound loses pliability and bacteria colonize the wound.

Infection

Infection of a wound is the principal cause of delay in healing. Infection is either primary, caused by organisms introduced by the traumatic agent, or secondary, produced by organisms subsequently admitted inadvertently. By the time many wounds are seen by the surgeon they are already needlessly contaminated by the overly zealous performance of first aid. The sight of blood arouses the overwhelming urge to "do something," and it requires considerable restraint to do nothing more than to apply a dressing at the scene of injury. Furthermore, each change of dressing introduces the risk of contamination. Lowry and Curtis have observed succinctly that "inspection means infection." [25]

Immediately after injury, contamination will be limited mainly to the exposed tissue surfaces. This important distinction between tissue contamination and infection

was first logically expounded by Friedrich.[20] With the passage of time, tissue contamination becomes wound infection. This incubation period has been said to be about six hours, but undoubtedly it varies considerably. During this period the surgeon has the opportunity to convert a contused, contaminated wound into an excised, surgically clean one. Since bacteria require time to multiply, the opportunity for survival of bacteria can be greatly decreased by depriving them of an avascular substrate. The remaining organisms are then incapable of multiplication when subjected to the defenses of viable tissue. Débridement therefore serves the dual purpose of interrupting bacterial proliferation and expediting the elimination of devitalized material.

Types of Wounds

It is difficult to standardize the technique of débridement, since this technique must vary according to the type of wound, the traumatic agent, and the environment. Each wound has an individuality which will tax the surgeon's ingenuity. Injuries caused by low-velocity agents usually are relatively clean, with limitation of destruction to the tissues actually in contact with the traumatizing object, and to the tissues devascularized by injury to major vessels. Conversely, high-velocity projectiles will cause much greater destruction.[21,22] This has been demonstrated by high-speed motion pictures. The rapidly moving object has a great kinetic energy, and when it encounters an obstruction it not only cuts a path but dissipates energy with an explosive effect, propelling tissue from its path in a radial direction. The tissues thus affected in turn become secondary projectiles with velocities of an appreciable fraction of that of the primary missile. This complex of forces produces a photographically demonstrable cavitation many times the diameter of the primary projectile. This cavity collapses with an elastic recoil, the degree depending upon the character of the local tissues. Destruction of tissue, then, is much wider than might be anticipated on casual observation.

Various tissues give evidence of variable tolerance to the destructive force. Skin, because it is elastic and vascular, will tolerate a considerable insult, and will therefore survive except for a narrow margin about the wound. This is fortuitous, since preservation of the skin is important to early healing. Subcutaneous tissue tolerates trauma poorly, and if it is injured it must be more widely removed. Muscle is most vulnerable, and will be extensively devitalized by injury. Tendons, fascia, and nerves, fortunately, are highly resistant to trauma.

Technique

The method of débridement must, as we have noted, conform to the type of injury at hand. Excision is necessary in lacerations, penetrating and perforating wounds, avulsions and human or animal bites. Although the extent of excision will vary according to the nature and extent of the injury, the principle remains the same: that of enlargement of the wound, total exploration, sharp aseptic excision of all tissue which is devitalized (or the circulation of which is so precarious that it will be an easy prey to infection), removal of accessible foreign material, adequate hemostasis, and thorough irrigation of the wound with copious quantities of isotonic solution of sodium chloride.[22]

It may appear naïve to discuss in detail the techniques of managing a wound. Kennedy [23] has reminded us, however, that "the care of traumatic wounds is the most common form of surgical treatment. It is frequently carried out indifferently." For purposes of example, the surgical revision of a recent wound caused by a high-velocity missile will be described.

It is axiomatic that débridement, for best results, must be done before contamination becomes infection. What has been termed the "golden period" lasts for about six hours. However, since this is relative, to invoke the six-hour rule and thus to permit

unnecessary delay of treatment is inexcusable. Excision deserves all the precautions which attend major surgery. It will follow, then, that débridement usually should be done in the operating room where major surgery is done, since emergency-room facilities will not often meet the needs for such exacting care. It is important to recall that organisms introduced from within the hospital may be much more virulent than those which the patient brought with him. It is an almost universal error to take a preliminary glance at the wound in the examining room without the protection of a mask. This is interpreted as a formal invitation by the ubiquitous and resistant Staphylococcus.

The surgical accouterments must of course include gowns, gloves, and full surgical drapes. After preliminary aseptic inspection, the wound should be packed with gauze, and left so while the surrounding part is shaved and prepared. With the wound still protected, preparation of the contiguous part is followed by an unattenuated 10-minute scrubbing with hexachlorophene soap. The use of skin antiseptic agents may be debated, but if they are used, they should be carefully excluded from the wound. The wound should then be outlined with towels and, after the surgeon has changed gloves, it may be unpacked. Copious irrigation with isotonic solution of sodium chloride not only washes out visible debris, but also reduces bacterial contamination by the simple device of dilution. This type of irrigation is too often neglected. It should be done lavishly. A full surgical drape is next applied, and members of the operating team are freshly gowned and gloved. Except for wounds of the hand, a tourniquet usually is not needed, but it is convenient to apply a pneumatic cuff, to be inflated in the event of troublesome bleeding.

Excision of the wound may then proceed. The objectives of débridement are (1) to remove all devitalized tissue, or that which is in jeopardy, (2) to open the wound widely for inspection of all recesses, (3) to remove accessible foreign material, and (4) to control bleeding, since collections of blood and serum act exactly as does avascular tissue. It must not be forgotten that the primary aim of débridement is removal of dead tissue, and, although a secondary purpose frequently may be preparation for delayed primary closure and future reconstructive surgery, conservation of tissue for these purposes must not influence the extent of primary débridement. Inattention to this concept is a frequent precursor of infection of a wound.

The first step in excision is enlargement of the wound. The extent of the deep destruction may be all out of proportion to the apparent surface injury. Incisions in the skin should parallel the long axis of the limb, except across flexion creases, where "Z" incisions are used. When perforating missile wounds are at hand, it is easier to begin with the larger wound of exit. Excision of skin must be economical, with sacrifice of no more than 2 to 3 mm. about the defect, in continuity with the incision. This will greatly facilitate closure.

From this point, the wound is incised, examined, and excised by layers. Excision en bloc is ideal, but seldom practicable. Because it is vulnerable, subcutaneous tissue must be excised more generously, the extent being determined by the limit of the extravasation of blood within the fat. Excision of fascia can be limited to obviously damaged tissue, but fascia must be incised widely in the direction of its fibers to expose all recesses and to relieve tension in closed compartments. This procedure will expose the muscle layers, which are then excised successively.

It is in this area that greatest judgment is necessary. The criteria of viability of muscle are subtle and difficult to convey. They have been evaluated recently by Scully, Artz, and Sako,[24] who found the best clinical index of viability to be the consistency of the muscle. Inviable muscle rapidly becomes "mushy." Significant also

are the ability of muscle to contract under mechanical stimulation and its ability to bleed. The least reliable sign is the color of the muscle. Because muscle is massive and because it is a good medium for bacterial support, it is imperative that muscle excision be adequate.

Periosteum probably should not be sacrificed unless it is severely contaminated. Opinions vary as to the amount of bone that should be discarded. Any bone which has periosteal attachment should be preserved, and it has been recommended that free fragments of bone be replaced, or that they be milled and used as chip grafts.[22] This process is thought by many authors to be hazardous.

Tendons deserve preservation in spite of contamination, and certainly should never be sacrificed if they are not severed.

Débridement of joints should be meticulous, with wide arthrotomy, removal of debris and fragments of cartilage, replacement of only large articular fragments, and closure of the capsule and ligaments without drainage.

Excision may be moderate in the hand and foot, in view of the lack of large muscle masses in those areas. Restraint must be used in the search for elusive metallic foreign bodies. In the hands and face, unless they have lodged superficially, they can be safely ignored. In areas in which clothing has been perforated, removal of metallic foreign bodies is more important. Those which are relatively inaccessible do not warrant extensive dissection for removal, unless they lie in juxtaposition to vital structures.

The initial care of wounds recently has been extended to include the repair of nerves and vessels. Nerves which are not severed should be cleansed gently and covered. Those which are cut may be carefully repaired if the wound is clean, treatment is immediate, anastomosis is possible without tension, and sufficient coverage is available. These exacting criteria will not often be met, and repair of the nerves will have to be delayed until healing of the wound is complete.

Surgery of blood vessels has made great strides since World War II. It is now unjustifiable to sacrifice any major vascular channel which conceivably can be reconstructed. It is equally important, in the event of damage to main vessels, that collateral channels be preserved scrupulously. The ideal method of repair is of course end-to-end suture of a cleanly lacerated artery. This ideal is not frequently realized, and some alternative must be utilized. Experience during the Korean conflict demonstrated the adequacy of autogenous saphenous and basilic-vein grafts as arterial substitutes. Employed for traumatic repair, grafts of this type, because of the external muscular support in the extremity and the adequacy of the distal portion of the arterial tree, are not susceptible to aneurysmal dilatation, and are thought by many to be the first choice. Other devices of course are available. It is now recognized that many failures after arterial repair in trauma are the results of venous inadequacy. When a major concomitant vein also is damaged, continuity of the vein should be restored.

After repair, muscle covering must be provided for bone, arteries, and nerves whenever this is feasible.

Since it is intimately related to the problem of débridement, wound closure deserves brief consideration. Primary wound closure is specifically contraindicated in war surgery. When primary closure is done for wounds of civilians, it requires the greatest judgment. The advisability will depend upon the lapse of time since injury, the degree of contamination, the condition of the patient, the thoroughness of the excision, the state of the blood supply, the completeness of hemostasis, the possibility of closure of the wound without tension or dead space, and the certainty of continuous observation for a period of 7 to 10 days. If any of these considerations is open to doubt, it is far wiser to leave the wound

open in anticipation of delayed primary closure than it is to proceed.

Certain clearly defined exceptions to this principle include wounds of the scalp, and especially those with intracranial extension, sucking wounds of the chest and wounds of the face and hands. Wounds of the scalp must be closed primarily. Wounds of the face may permit extension of the time limit to as much as 48 hours. Wounds of the hands present special problems of coverage of tendons. During World War II and early in the Korean episode, wounds of this nature were closed primarily, but often with infection rates approaching 90%. Later in the Korean experience wounds of the hands were left open for delayed closure without severe loss of tendon function. In civilian practice, wounds of the hands probably should be closed loosely, with adequate provision for drainage.

Lowry and Curtis [25] found that even when complete excision en bloc was done, 50% of war wounds which were closed primarily became infected. Although civilian practice will permit more latitude, primary nonsuture is preferable in all but ideal circumstances. It is a technique which is assiduously avoided by many surgeons, perhaps because they have a compulsive regard for neatness.

Primary suture has almost no advantage over delayed primary closure. This latter term and the techniques concerned were first widely used by Depage during World War I. Although delayed primary closure was virtually forgotten between wars, it is now firmly established in both military and civilian surgery. It is predicated upon complete initial surgery, resulting in a clinically clean wound. A débrided wound which has been provided with drainage and the exposed surfaces of which have been covered with a layer of fine mesh gauze—specifically not packed—and supported by a large occlusive dressing for a period of four or five days will exhibit a glazed fibrin membrane. This membrane delimits the exudative phase of healing, and is the cue for closure. The peak of healing will occur when closure is accomplished on the fourth or fifth day.

Although lesser successes may be expected up to 10 days, the progression of the proliferative or fibrotic phase of healing after five days causes the wound to lose pliability, permits formation of granulation tissue, allows epithelial fixation, and permits the establishment of a fixed bacterial flora. Dead space is then difficult to obliterate; the skin is hard to close, granulation contracture occurs, and infection is much commoner. Bick [4] aptly observed: "The days of proudly exhibiting 'good healthy granulation tissue' have become as archaic as have the days of 'laudable pus'." The technique has been called advisedly "delayed primary closure," since it has all the advantages of primary closure, and may be done with almost no revision of the wound. The applicability of the technique depends upon the exercise of sound judgment, since late secondary closure is greatly preferable to enclosed spreading infection.

Enzymatic Débridement

Débridement in the face of established infection until recently has been hazardous. It is now possible, with appropriate antibiotic coverage, to pursue judicious excision. It should be limited to the removal of necrotic material and collagenous matter unaffected by natural enzymes. It is not possible clearly to delimit normal tissue and produce a (surgically) clean wound. Recognition of the function of naturally occurring enzymes led to search for means to facilitate the action of the enzymes. Exogenous enzymatic débridement is still more promising than practical. Reported results have been inconstant because of lack of understanding of the limitations and proper methods of use of the enzymes in question.

Even the most potent enzyme will not act with clinical adequacy if it is applied to a lesion possessing chemical and physical circumstances unfavorable to the activity of the enzyme. Many failures can be at-

tributed to failure to select an enzyme suitable to the substrate, and failure to modify the environment of the wound to permit action of the enzyme. This presupposes a knowledge of the potential of each enzyme and the circumstances which will abet or inhibit the function of the agent. The common causes of failure are as follows:

1. Lack of a potent enzyme resulting from improper storage or use of an inappropriate vehicle.
2. Use of enzymes against improper substrates, since enzymes are tissue-specific.
3. Use of other chemicals for other therapeutic purposes which destroy or inhibit the enzyme. Examples of this are heavy-metal antiseptic agents and hexachlorophene (G-11).
4. Failure to restrain bacterial growth.
5. Drying of substrate.
6. Persistence of foreign material or sequestra.
7. Inaccessible loculation of pus, as in osteomyelitis of cancellous bone.

Streptokinase, produced from hemolytic streptococci, reacts with plasminogen to produce plasmin, which in turn is fibrinolytic. Streptodornase, from the same source, depolymerizes deoxyribonucleic acid, the viscous breakdown product of pus cells, and produces a more fluid exudate. The combination of these is extremely effective against fibrinopurulent exudates, but not against collagen or tissue protein. Moreover, streptokinase and streptodornase require a pH of about 6, whereas that of pus usually is much more alkaline.

Crystalline trypsin is recovered from animal pancreas, and is a potent proteolytic agent. It works best when necrotic tissue needs to be removed. It also requires a pH of about 6. It has a short activity, and is rapidly destroyed by bacteria, which means that it must be used in conjunction with antibiotic agents. Since it is a protein, trypsin provokes an antibody response and loses effectiveness after several days of use.

There are no naturally occurring collagenases outside the gastrointestinal lumen. Therefore, skin, tendons, fascia, and connective tissue are very slowly removed naturally. Pepsin applied topically requires an extremely acid pH, which is difficult to maintain. Papain, of vegetable origin, is an excellent collagen digestant, but requires sodium salicylate as an activator, in concentrations which produce generalized toxicity. Collagenases of clostridial origin are being developed and are by far the most effective.

Enzymes, used properly, will become important adjuncts in the management of infected and necrotic wounds, but they never will be substitutes for surgical débridement.

Lowry and Curtis[25] listed the errors which most commonly prejudiced prompt healing of wounds during World War II:

1. Improper concept of débridement.
2. Sacrifice of too much skin.
3. Plugging of the wound with petrolatum-gauze packing.
4. Primary suture of débrided wounds in doubtful situations.
5. Tampering with or manipulation of wounds either before or after débridement.
6. Insufficient immobilization of débrided wounds.
7. Almost total ignorance of the procedure of delayed suture, in spite of wide use and detailed description of the technique during the First World War.

It is interesting that these points are almost identical with those listed by Ireland[26] in 1919.

Mayo Clinic.

REFERENCES

1. Desault, cited by Woolsey, J. H.: Débridement, Am. J. Surg. 82:179-182 (July) 1951.
2. Larrey, J. D., cited by Woolsey, J. H.: Débridement, Am. J. Surg. 82:179-182 (July) 1951.
3. Depage, A.: General Considerations as to the Treatment of War Wounds, Ann. Surg. 69:575-588 (June) 1919.
4. Bick, E. M.: Source Book of Orthopaedics, Ed. 2, Baltimore, The Williams & Wilkins Company, 1948.
5. Campbell E., and Colton, J. B., Jr.: Theodoric: Master Surgeon of the 13th Century, New York J. Med. 54:191-193 (Jan. 15) 1954.
6. Botello, L., cited by Hewlett, T. H.*
7. Pirogoff, I., cited by Yudin, S. S.: The Treatment of War Fractures of the Femur, Surg. Gynec. & Obst. 78:1-8 (Jan.) 1944.
8. Dakin, H. D.: On the Use of Certain Antiseptic Substances in the Treatment of Infected Wounds, Brit. M. J. 2:318-320 (Aug. 28) 1915.

9. Hewlett, T. H.: Débridement, Am. Pract. & Digest Treat. 3:562-568 (July) 1952.

10. Friedrich, P. L., cited by Woolsey, J. H.: Débridement, Am. J. Surg. 82:179-182 (July) 1951.

11. Gray, H. M. W.: Treatment of Gunshot Wounds by Excision and Primary Suture, Brit. M.J. 2:317 (Aug. 28) 1915.

12. Lewis, D. D.: Débridement, J.A.M.A. 73: 377-383 (Aug. 9) 1919.

13. Pool, E. H.: War Wounds: Primary and Secondary Suture, J.A.M.A. 73:383-387 (Aug. 9) 1919.

14. Koch, S. L.: The Immediate Treatment of Compound Injuries, Illinois M.J. 67:40-43 (Jan.) 1935.

15. Orr, H. W.: Determining Factors in the End-Results Following War Wounds and Compound Fractures, Bull. New York Acad. Med. 18: 237-245 (April) 1942.

16. Trueta, J.: Treatment of War Wounds and Fractures with Special Reference to the Closed Method as Used in the War in Spain, New York, Paul B. Hoeber, Inc., 1940.

17. Trueta, J.: The Principles and Practice of War Surgery, Ed. 3, London, Hamish Hamilton, Ltd., 1946.

18. Meroney, W. H.: Uremia-like Symptoms Not Due to Uremia in Battle Casualties, J.A.M.A. 158:1513-1516 (Aug. 27) 1955.

19. Vandenbos, K. Q.: Wound Shock and Débridement, A.M.A. Arch. Surg. 75:707-708 (Nov.) 1957.

20. Friedrich, P. L.: Die aseptische Versorgung frischer Wunden, unter Mittheilung von Thier-Versuchen über die Auskeimungszeit von Infectionserregern in frischen Wunden, Arch. klin. Chir. 57:288-310, 1898.

21. Ochsner, E. W. A., Jr.: Experimental Wound Ballistics, in Recent Advances in Medicine and Surgery, U.S. Department of Defense, Army Medical Service, 1954, Vol. 1, pp. 222-229.

22. Pulaski, E. J.: War Wounds, New England J. Med. 249:890-897 (Nov. 26); 932-938 (Dec. 3) 1953.

23. Kennedy, R. H.: Present-Day Early Care of Traumatic Wounds, S. Clin. North America 35: 355-367 (April) 1955.

24. Scully, R. E.; Artz, C. P., and Sako, Y.: An Evaluation of the Surgeon's Criteria for Determining the Viability of Muscle During Débridement, A.M.A. Arch. Surg. 73:1031-1035 (Dec.) 1956.

25. Lowry, K. F., and Curtis, G. M.: Pertinent Factors Influencing Repair in Traumatic Wounds, Am. J. Surg. 78:781-792 (Nov.) 1949.

26. Ireland, M. W., cited by Lowry, K. F., and Curtis, G. M.[25]

The Management of the Ruptured Aortic Aneurysm

JOHN STORER, M.D., and RALPH C. SMITH, M.D., Cleveland

The lethal potential of arteriosclerotic aneurysms of the abdominal aorta has been clearly demonstrated. Because of this and the disabling symptomatology often related to the aneurysm, many surgical attacks have been devised. The ideal treatment consists of excision of the aneurysm and restoration of vascular continuity by the insertion of a graft. This form of therapy has been made possible by the pioneering effort of DeBakey, Cooley, and Creech, and Bahnson and DuBost.[1-3] Other forms of therapy have been abandoned in favor of this ideally definitive method.[4] A reduction in operative mortality to 5% has followed as greater surgical experience has been acquired.

The detection of an abdominal aneurysm is accomplished during the routine physical examination by simple palpation. With the patient lying on his back, even the obese abdomen can be accurately assessed as regards the presence of a pulsating mass. As in all things, a high index of suspicion is the most valuable tool in the physician's kit. Backache is such a frequent symptom that aneurysm should be excluded routinely when examining a patient for this complaint. Many aneurysms are first detected by the radiologist after "back studies," flat films, or intravenous pyelography.

The natural progress of an aneurysm is on to rupture, and this usually within a few years of detection.

Since the aorta is retroperitoneal, the ruptured aneurysm may be contained by the peritoneum for a variable period of time. When the peritoneum is fractured by the enlarging hematoma, fatal issue is at hand. The formerly contained blood vascular system has released its content into the abdominal cavity. However, before this situation occurs, a set of swiftly moving circumstances may be effected and certain death averted. Since this time interval is an unknown factor, the need for a rapid decision is obvious. Once the diagnosis has been made, the aorta above the aneurysm must be the target for immediate attack. As our experience with ruptured aneurysms has increased, the plan of siege has been altered to carry the patient through to a swift and safe termination. All patients have abdominal pain varying in severity from mild to profound. The initial pain may be so intense as to precipitate syncope. Irritation of the sigmoid colon by the blood extravasating through the mesentery frequently causes diarrhea. The blood may dissect along the retroperitoneal tissues and present in the inguinal canals, leading to a mistaken diagnosis of incarcerated inguinal hernia. A pulsatile mass may be palpated through the rigid abdominal wall. On occasion this mass will literally increase in size under one's eye. The femoral pulses remain palpable unless they have been previously abolished by an obstructive arteriosclerotic process.

As soon as the diagnosis is made, we do not believe there is time or need for elaborate diagnostic procedures. A blood count, urinalysis, blood typing, and cross matching are the only laboratory procedures requested.

The patient is taken to the operating room immediately. Two "cutdowns" are done and blood started. The method of anesthetic induction is of great importance. Early in our experience, little attention was paid to this phase of the anesthetic management. In one instance the patient bore down, in-

Submitted for publication May 19, 1959.

From the Department of Thoracic and Cardiovascular Surgery, Huron Road Hospital.

Incisions used for managing a ruptured aneurysm.

creasing his intraabdominal pressure so greatly that the large, easily visible pulsatile mass flattened out, and the patient died forthwith. This led to the use of neuromuscular blocking agents prior to induction of anesthesia. The patient is completely paralyzed by succinylcholine chloride (Anectine). Endotracheal intubation is then rapidly accomplished, and the patient is anesthetized. This may seem somewhat cruel but it has been most helpful in controlling this critical phase.

The abdomen and left chest are then draped and prepared in the routine manner and a lower left rectus incision made. The diagnosis is thereby confirmed. Without any further abdominal exploration, a submammary incision is made in the left chest. The pleura is entered through the sixth intercostal space. The aorta is isolated just above the diaphragm and a Satinsky clamp placed around it in a position of readiness. Its jaws are not closed, however. The abdominal incision is then lengthened from the ensiform cartilage to the pubis, the viscera packed off, and dissection begun. Our immediate surgical attack centers on isolation of the aorta above the aneurysm, which is in most cases below the renal arteries. After the posterior parietal peritoneum has been incised, our primary effort is localized to the space between the aorta and inferior vena cava just below the point of entry of the left renal vein. This area we have dubbed the "friendly space." Here the vena cava and aorta are usually not adherent, and dissection can be started posteriorly and carried around the aorta. Blunt dissection with the index finger will enable the surgeon to encircle the vessel in a matter of a few minutes. The Satinsky clamp is removed from the thoracic aorta and placed across the abdominal aorta at the point of dissection. Again, the jaws are left open. Removal of the aneurysm is carried out in the fashion which has been described numerous times by the previously mentioned authors. Aortic continuity is reestablished by the insertion of a preclotted elasticized Dacron graft. Restoration of blood volume as quickly as possible is accomplished during the surgical procedure. If at any time during the dissection bleeding occurs which seriously interferes with continued manipulation, the aorta is occluded in the chest by closing the jaws of the Satinsky clamp. As soon as the aorta can be encircled in the abdomen the thoracic aorta is unclamped and the abdominal aorta occluded. We have seen no serious impairment of renal or hepatic function by clamping the aorta in the chest for a period of 10 minutes.

Transthoracic control of the aorta in treating ruptured aneurysms was first suggested by Javid[5] in 1956. Further experiences with this method was reported by Merendino.[6] It is an extremely helpful maneuver in controlling the alarming hemorrhage which may ensue during the course of dissection prior to isolation of the abdominal aorta above the aneurysm. We have also used it in many instances when there has been uncontrollable abdominal aortic bleeding from other causes. The added morbidity from left thoracotomy is slight

and the postoperative chest wound is easily handled.

Hereinafter are briefly recorded a few experiences with ruptured aneurysms, which have helped to crystallize our present concepts concerning this problem.

CASE 1.—A 49-year-old white man was transferred to Huron Road Hospital with a diagnosis of ruptured abdominal aortic aneurysm. He complained chiefly of diffuse abdominal pain which was sharp and continuous. On examination, the patient was noted to be in a state of severe shock. His blood pressure was 70/50 and pulse rate 120. A tender pulsatile mass was visible in the abdomen. The femoral pulses were palpable. The left lower extremity had been amputated several years previously. The patient was taken to the operating room, where he was prepared in the routine fashion. During the excitement stage of his general anesthesia, he bore down with a closed glottis and visibly increased his intra-abdominal pressure. The pulsatile mass "flattened out," and no longer were pulsations visible. Rapid entry was made into the abdominal cavity. Free blood was found throughout the peritoneal cavity, and a large puncture site in the aortic aneurysm and peritoneum was observed. Pressure was made on the aorta above the aneurysm, and blood rapidly pumped into several venipuncture sites. His blood pressure rose from an imperceptible level to 90 mm. Hg. An attempt was made to encircle the aorta with a Satinsky clamp, but the patient died shortly thereafter, presumably from the blood loss sustained during this maneuver.

It occurred to us at this time that transthoracic control of the aorta was necessary if a salvage of this type of case was to be obtained. Left thoractomy with control of the thoracic aorta seemed to represent the avenue of further exploration. Shortly thereafter we had an opportunity to test this postulate.

CASE 2.—A 65-year-old white man was admitted to Huron Road Hospital with a chief complaint of abdominal pain, nausea, and vomiting of 48 hours' duration. His blood pressure was fairly stable at 120/80, though his pulse was 110. His abdomen was distended and tender, and at least one observer thought he felt a pulsatile mass. He was observed for a period of 24 hours, during which time there was little change in his condition. At the end of this time, however, his condition became worse. There was an increase in the abdominal distention and the size of the abdominal mass. The mass was continuous over the right inguinal region. A general surgical consultant examined the patient at this point and made a diagnosis of ruptured abdominal aortic aneurysm with dissection of blood into the right inguinal region. The possibility of incarcerated inguinal hernia was to be excluded. Many observers favored the latter diagnosis. The patient was taken to the operating room, where abdominal exploration confirmed the presence of a rupture aortic aneurysm. There was a large amount of blood in the retroperitoneal area, which had dissected down to the right inguinal region. The posterior parietal peritoneum was dissected slightly, in order to evaluate the extent of the aneurysm. This slight dissection was suddenly met with a great rush of blood through the puncture site in the aneurysm. The operator inserted his hand in the aneurysm, through the puncture site, and controlled bleeding by inserting the index finger up into the aorta. Blood was pumped in under pressure, and other supportive measures were instituted after bleeding was controlled. The operator then withdrew his finger from the aorta, and the first assistant rapidly inserted his hand and finger in the same area. The left chest was then quickly prepared and draped, and a left thoracotomy was done. The thoracic aorta was isolated and clamped. Then, within two minutes, the abdominal aorta was isolated and clamped above the aneurysm, and the thoracic aorta unclamped. A routine dissection of the aneurysm was carried out and aortic continuity reestablished by insertion of a homograft. The patient was returned to his room in good condition.

That evening his condition remained good, but there was evidence of a right femoral arterial obstruction. An embolus was removed from the femoral artery at the level of the bifurcation of the deep and superficial femoral arteries. His condition was good following this procedure.

The patient's postoperative course was uneventful, with the exception of some difficulty resultant from bronchial asthma and bronchiectasis.

On the 11th postoperative day, when he was in excellent condition, he suddenly developed massive hematemesis. He was placed on the management of bleeding ulcer, as advocated by Marshall, which promptly controlled it.[7] However, 24 hours later he again had a massive hemorrhage, which caused death. An autopsy disclosed the presence of a large prepyloric ulcer crater on the posterior surface of the stomach. A pipestem artery protruding into the middle of the crater was responsible for the exsanguinating hemorrhage. The aortic graft was in excellent condition, and there was no leak at the anastomotic junction.

CASE 3.—A 69-year-old white woman was seen in consultation, and a diagnosis of uncomplicated arteriosclerotic aneurysm of the abdominal aorta established. She was apprised of the diagnosis and informed of the necessity for surgery. She was placed on the "semiemergency admission list" for hospitalization and sent home. Twenty-four hours

later she developed diarrhea. This was rapidly followed by nausea, vomiting, back and abdominal pain, and prostration. She was brought to the emergency room of Huron Road Hospital after a telephone conversation with her daughter, who had informed us of the above facts. Her blood pressure was 140/80, pulse rate 92, and respirations 26. (Her family physician had treated her for hypertension for several years.) She was in acute distress, with cold, moist skin, and complained bitterly of low back and abdominal pain. In addition, she vomited frequently during the examination. The abdomen was diffusely tender. The pulsatile mass had assumed an entirely different pattern from that noted on the previous day's examination. The borders of the mass were indistinct, where previously they had been sharp. It appeared to be less confined, although pulsations remained fairly prominent. The femoral arteries were palpable. A diagnosis of ruptured aneurysm of the abdominal aorta was made, and the patient was taken to the operating room. A left rectus incision was made and the diagnosis confirmed. The left chest was opened through a submammary incision. The aorta was isolated above the diaphragm and a Satinsky clamp placed around it, but the jaws were not closed. The abdominal incision was then extended from the ensiform cartilage to the pubis and dissection of the aneurysm carried out. The thoracic aorta was clamped and dissection carried around the abdominal aorta, and a Satinsky clamp was placed over the aorta just proximal to the aneurysm and distal to the renal arteries. This was followed by release of the thoracic aorta, which was not clamped for more than five minutes during this maneuver. A routine excision of the aneurysm was accomplished and a graft inserted. The wounds were closed and a thoracotomy tube brought out to an under-water seal. The entire operating time for this procedure was 2 hours and 15 minutes.

Her convalescence was uncomplicated, and she was discharged two weeks after admission in good condition. This experience has been repeated successfully in five instances.

Conclusions

The ideal treatment of an arteriosclerotic aneurysm of the abdominal aorta is excision and grafting. This is not a technically difficult feat in the uncomplicated case. The good operative result and the low mortality rate associated with surgical treatment suggest this therapy be recommended in all but unusually complex cases. Certainly the aneurysm should be thought of as a malignant lesion. One should not seek an illogical deterrent to surgery any more than if one were dealing with a carcinoma of the large bowel. Nothing is so unrewarding as to carry these patients on conservative therapy to the point of rupture.

There is another group of patients in whom the aneurysm has been undetected. This allows a fairly significant population of potential ruptured aneurysms. Therefore this diagnosis must be considered when evaluating the acute abdomen in every patient past the fourth decade. When the diagnosis of ruptured aneurysm is made, the patient must be subjected to surgery as soon as possible. Certain suggestions have been made which have been helpful in carrying the patient through this catastrophe to safety.

10900 Carnegie Ave. (6).

REFERENCES

1. De Bakey, M. E.; Cooley, D. A., and Creech, O., Jr.: Aneurysm of the Aorta Treated by Resection, J.A.M.A. 163:1439-1443 (April 20) 1957.

2. Bahnson, H. T.: Surgical Treatment of Abdominal Arteriosclerotic Aneurysms, S. Clin. North America 36:983-993 (Aug.) 1956.

3. Dubost, C.; Allary, M., and Oeconomos, N.: Resection of Aneurysm of Abdominal Aorta: Reestablishment of Continuity by Preserved Human Arterial Graft, with Result After Five Months, A.M.A. Arch. Surg. 64:405-408 (March) 1952.

4. Blakemore, A. H.: Abandonment of Banding and Wiring for Aneurysm, Surgery 41:861 (May) 1957.

5. Javid, H.; Dye, W. S.; Grove, W. J., and Julian, O. C.: Resection of Ruptured Aneurysm of Abdominal Aorta, Ann. Surg. 142:613-623 (Oct.) 1955.

6. Merendino, K. A.: Ruptured Abdominal Aneurysm: Transthoracic Control, Surg. Gynec. & Obst. 103:639-642 (Nov.) 1956.

7. Marshall, E. A., and Sass, M.: Peptic Ulcer: Treatment with Unrestricted Diet—Report of 1500 Cases, M. Times 83:552-557 (June) 1955.

Radiologic Features of Isolated Ventricular Septal Defects

EDWARD B. SINGLETON, M.D.; DAN G. McNAMARA, M.D., and DENTON A. COOLEY, M.D.,
Houston, Texas

The roentgenologic features of isolated ventricular septal defects depend upon size of the defect, amount of pulmonary resistance, and resulting direction and degree of the shunt. Fluoroscopy is indispensable in evaluating the physiologic alterations in all forms of congenital heart disease and should be a part of the radiologic evaluation of ventricular septal defects. Routine chest roentgenograms, including posteroanterior and right and left oblique with radiopaque contrast material in the esophagus, are equally important not only in determining the anatomical alterations but also in serving as a permanent record for comparison with subsequent studies. There are no pathognomonic radiographic characteristics of ventricular septal defects, but certain distinguishing features should be recognized. Because the alteration in cardiac configuration in ventricular septal defects as well as in other types of congenital heart disease is dependent upon pressure changes, we have devised the following classification in which the radiologic features are correlated with pressure in the pulmonary circulation and volume of intracardiac shunts.[1] This classification is useful in selection of patients for repair of ventricular septal defects in open cardiac techniques and has been derived from observations in a series of 150 surgically treated patients.[2] Thus, isolated ventricular defects may be classified as follows:

Received for publication April 28, 1959.

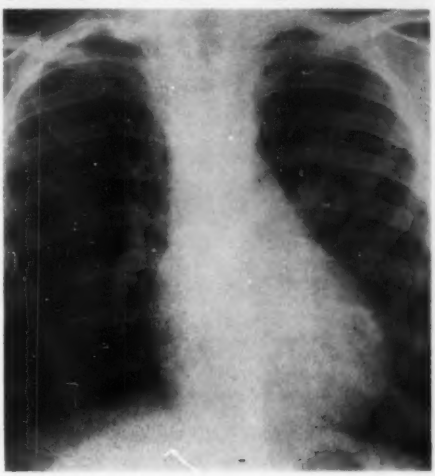
From the Department of Radiology and the Cardiac Clinic, Texas Children's Hospital, and the Cora and Webb Mading Department of Surgery, Baylor University College of Medicine.

1. Small defect with small left-to-right shunt and no pulmonary hypertension
2. Medium-sized defect with moderate left-to-right shunt and moderate elevation in pulmonary arterial systolic pressure (usually greater than 40 and less than 60 mm. Hg)
3. Large defect with large left-to-right shunt and moderately severe elevation in the pulmonary arterial pressure (usually greater than 60 and less than the systemic pressure)
4. Large defect with pulmonary arterial pressure equal to the systemic pressure (within 10 mm. Hg) and predominant left-to-right shunt
5. Large defect with predominant right-to-left shunt and pulmonary arterial pressure equal to the systemic pressure (within 10 mm. Hg).

Radiologic Considerations

The pertinent radiologic features consist of changes in size of the left and right ven-

Fig. 1 (Class 1).—Posteroanterior chest roentgenogram in a 7-year-old boy, showing heart of normal size and configuration and pulmonary vascularity within normal limits. At catheterization pulmonary artery pressure was 30/5 mm. Hg and systemic pressure 100/60 mm. Hg.



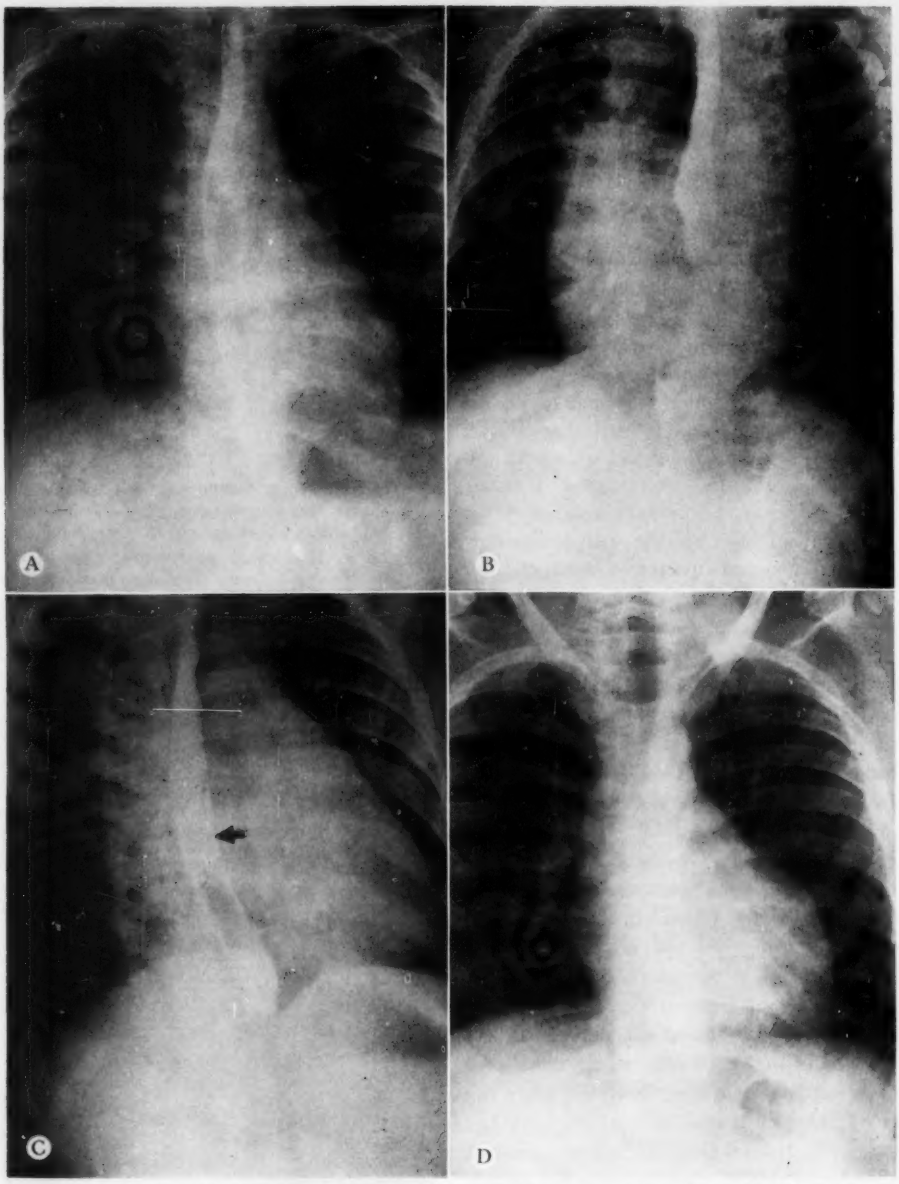


Fig. 2 (Class 2).—Roentgenograms in an 11-year-old boy. At catheterization his pulmonary artery pressure was 45/10 mm. Hg and systemic pressure was 125/75 mm. Hg. *A*, posteroanterior chest roentgenogram, showing heart of normal size and pulmonary vascularity slightly more prominent than normal. *B*, left anterior oblique projection, demonstrating slight left ventricular enlargement (arrow). *C*, right anterior oblique projection, showing questionable slight enlargement of left atrium (arrow). *D*, posteroanterior roentgenogram five months after operation, revealing normal pulmonary vascularity and less prominent pulmonary artery segment.

tricles and the left atrium and in the degree of pulmonary vascularity. In general, changes in these components are clear-cut and fall readily into the classification given above. Occasionally, however, the radiologic features of one classification merge with those of the next. This occurs in those cases in which the pulmonary arterial pressure borders on that found in the two adjoining classes.

1. *Small Defect.*—In small ventricular septal defects the interventricular shunt is accordingly slight; the roentgenologic appearance is within normal limits; the heart is of normal size and configuration, and the pulmonary vascularity is not appreciably altered (Fig. 1). This is particularly true of defects involving the muscular portion of the septum but also applies to small defects in the membranous portion.

2. *Medium-Sized Defect.*—With moderate-sized ventricular septal defects and with a moderate left-to-right shunt pulmonary vascularity is increased and the undivided pulmonary artery segment is prominent (Fig. 2). Abnormal hilar pulsations are not as a rule identified fluoroscopically. Left ventricular enlargement of varying degree is present and is identified in posteroanterior view by elongation or increased convexity of the outflow tract. In the left anterior oblique position left ventricular dilatation is detected by failure of the posterior portion of the cardiac silhouette to clear the spine when the patient is rotated into nearly lateral position. No set figure can be ascribed to the degree of rotation, since the habitus of the patient, the degree of inspiration, and the size of the right ventricle all affect it significantly. Of more importance is the impression gained by the experienced fluoroscopist who is able to take each of these factors into consideration. The majority of cases will show significant enlargement of the left atrium, but this is not always a detectable feature. This is seen to best advantage fluoroscopically with the patient in the right anterior oblique position and with the esophagus outlined by radiopaque material. The aorta is of normal size, as determined by the impression it makes upon the contrast material within the esophagus.

3. *Large Defect with Left-to-Right Shunt.* Large ventricular septal defects with large left-to-right shunt and with moderate elevation of pulmonary arterial pressure demonstrate the features previously mentioned with the additional evidence of right ventricular enlargement and greater dilatation of the pulmonary artery segment (Fig. 3). Right ventricular enlargement is best demonstrated with the patient in the left anterolateral position, the anterior chamber showing a greater convexity and approaching the anterior chest wall. The left ventricle is also obviously enlarged, and because of the combination of right and left ventricular enlargement the over-all size of the heart is moderately enlarged. The left atrium is also dilated and to a greater degree than that seen in the previous group. The pulmonary vascular markings are greatly accentuated and extend to the peripheral portions of the lungs. Abnormal hilar pulsations usually may be identified fluoroscopically.

4. *Large Defect with Equal Pressures.*—In large ventricular septal defects in which pressures in the pulmonary and systemic circulations are approximately equal (within 10 mm. Hg) and the shunt is predominantly left to right, the heart is usually large and dilated or may show only moderate increase in size (Fig. 4). Both right and left ventricular enlargement is evident, and there is usually no left atrial enlargement. The peripheral pulmonary branches may be diminished in size, with a correspondingly greater dilatation of the hilar vessels and undivided pulmonary artery segment. Because of the relatively greater increase in size of the right ventricle there may appear to be a decrease in the over-all size in comparison with previous radiographs. The roentgenologic appearance in these cases may therefore be misleading. The aortic knob may appear unusually small.

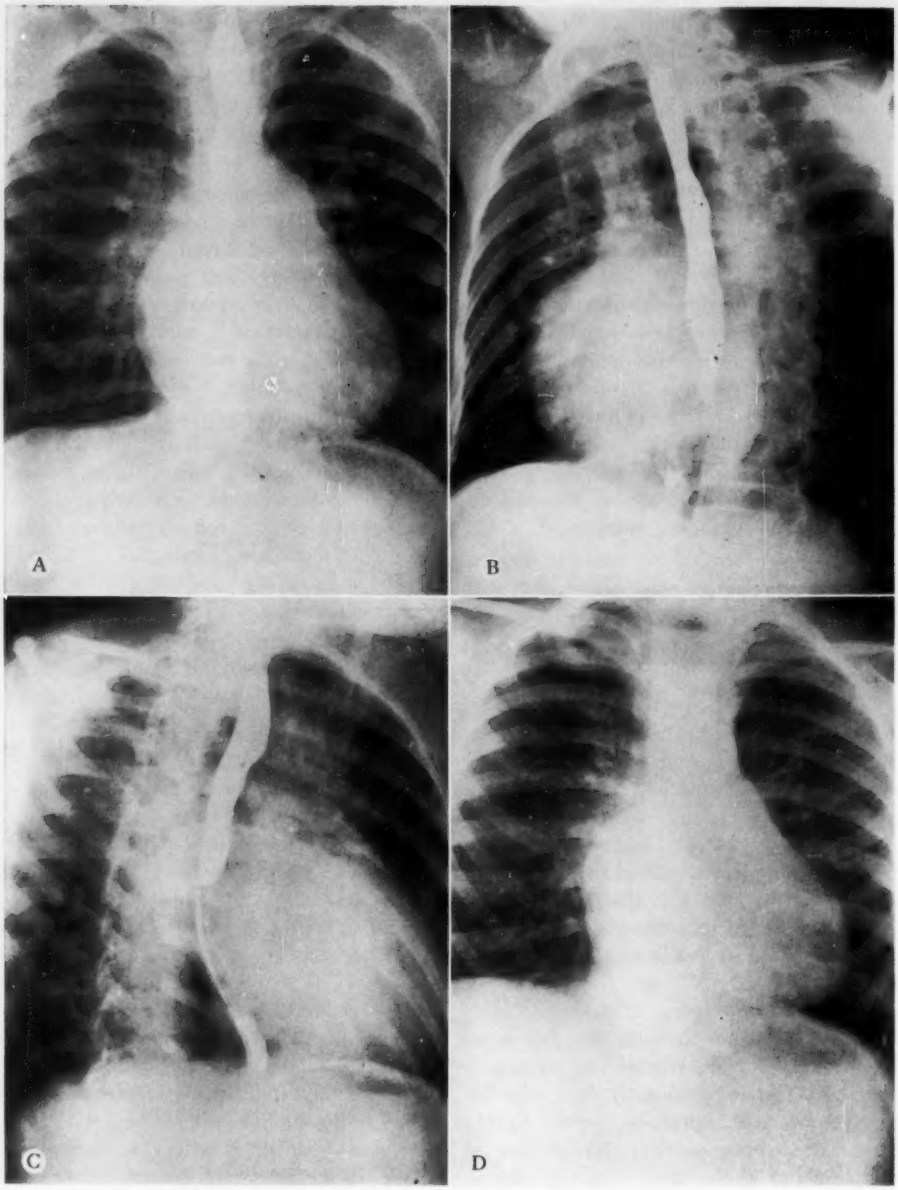


Fig. 3 (Class 3).—Roentgenograms in a 6-year-old girl who at catheterization had a pulmonary artery pressure of 85/50 mm. Hg and systemic pressure of 110/60 mm. Hg. *A*, posteroanterior chest roentgenogram, showing moderate cardiac enlargement, abnormally prominent pulmonary artery segment (arrow), and greatly accentuated pulmonary vascular markings. *B*, left anterior oblique projection, showing right and left ventricular enlargement. *C*, right anterior oblique projection, showing pronounced left atrial enlargement. *D*, posteroanterior roentgenogram four months after closure of defect, showing normal pulmonary vascularity and decrease in size of pulmonary artery segment.

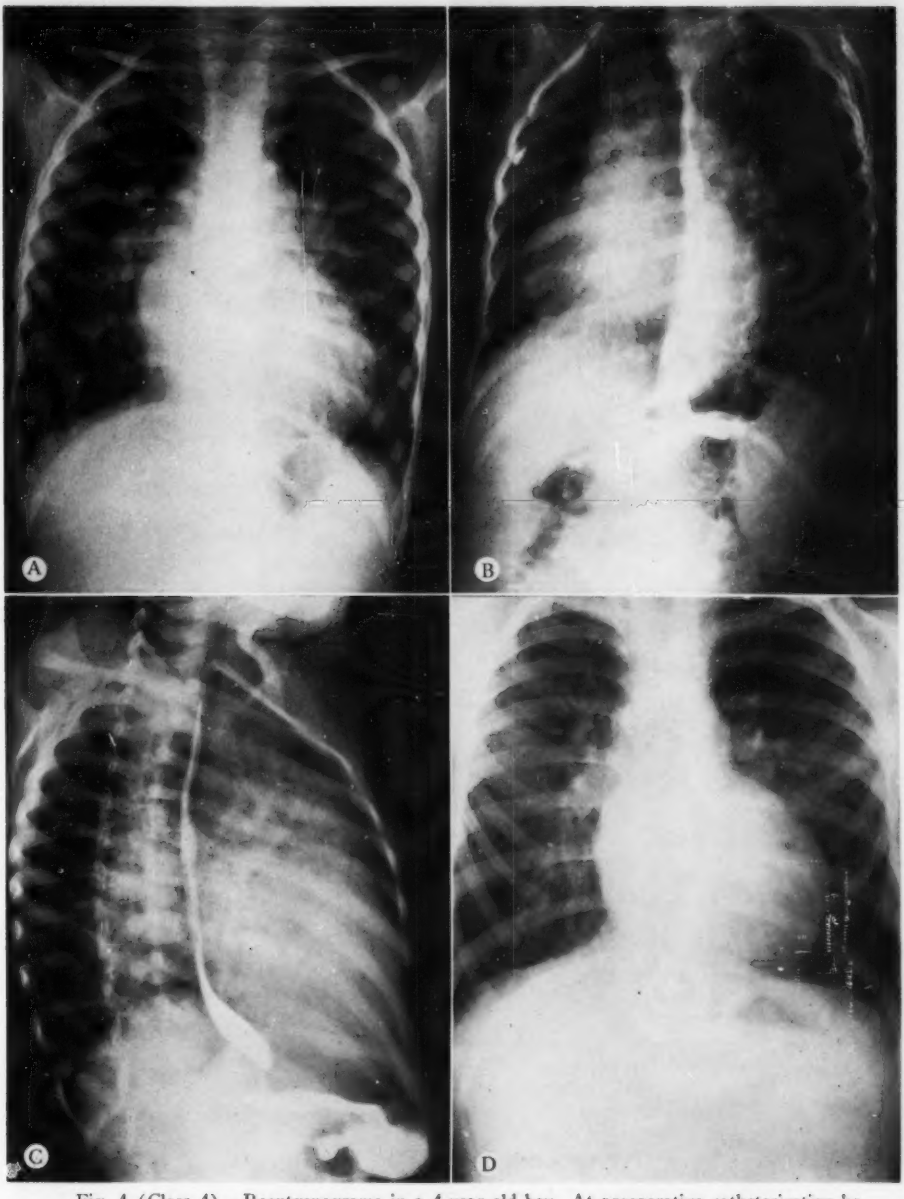


Fig. 4 (Class 4).—Roentgenograms in a 4-year-old boy. At preoperative catheterization he had a pulmonary artery pressure of 90/50 mm. Hg and systemic pressure of 92/40 mm. Hg. *A*, posteroanterior roentgenogram, showing moderate cardiac enlargement, abnormally prominent pulmonary artery segment, small aortic knob, and dilated hilar vessels with diminution in caliber of vessels in lung periphery. *B*, left anterior oblique projection, showing extensive right and left ventricular enlargement. *C*, right anterior oblique projection, showing no left atrial enlargement. At postoperative catheterization the pulmonary artery pressure was 36/10 mm. Hg and systemic pressure 105/50 mm. Hg. *D*, posteroanterior roentgenogram one year after operative closure of defect, showing decrease in heart size and essentially normal vascular markings.

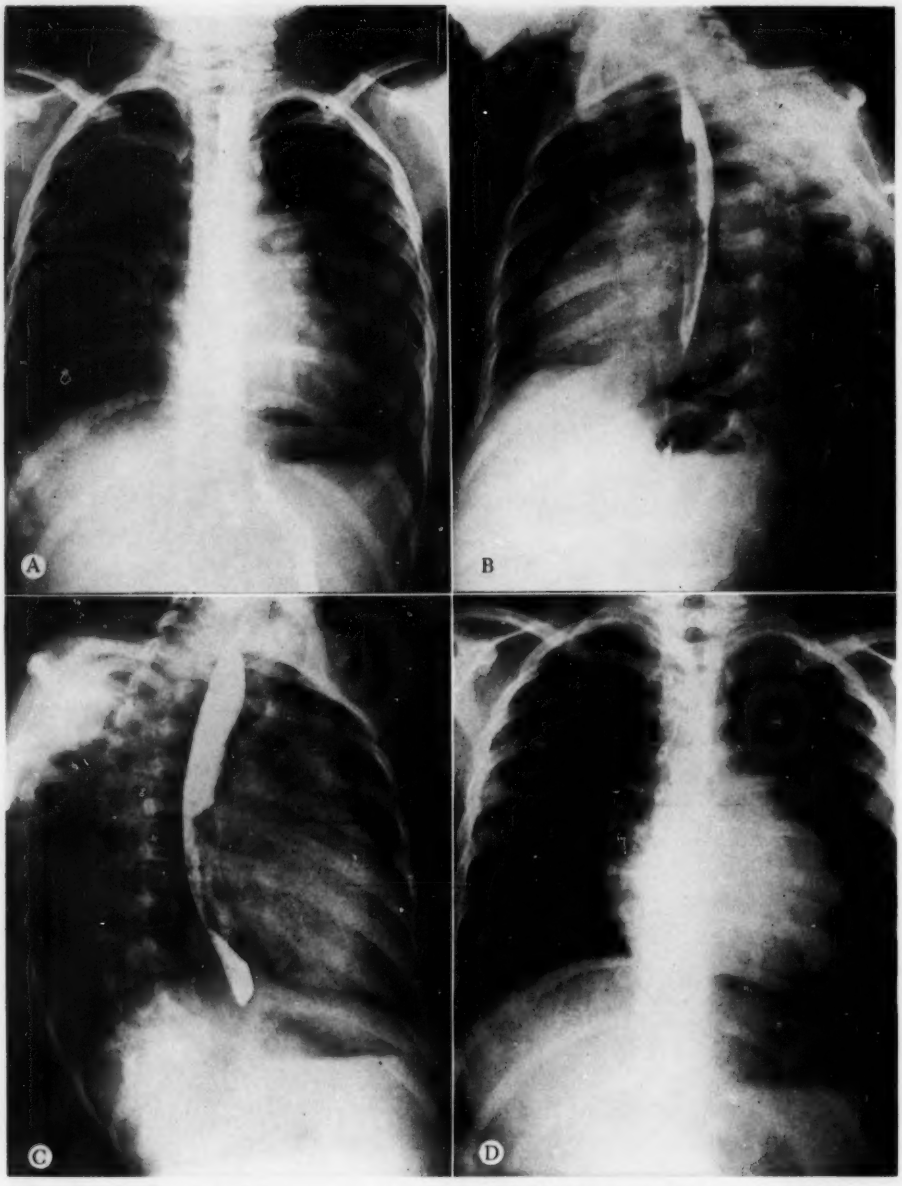


Fig. 5 (Class 5).—Roentgenograms in a 7-year-old girl who at preoperative catheterization had a pulmonary artery pressure of 100/56 mm. Hg and a systemic pressure of 110/55 mm. Hg. *A*, posteroanterior chest roentgenogram, showing normal-sized heart and abnormally convex pulmonary artery segment. Hilar structures are prominent, but peripheral markings are inconspicuous. *B*, left anterior oblique projection, showing evidence of right ventricular enlargement and questionable left ventricular enlargement. *C*, right anterior oblique projection, showing no definite left atrial enlargement. Postoperative catheterization revealed a pulmonary artery pressure of 125/62 mm. Hg and systemic pressure of 145/72 mm. Hg. *D*, posteroanterior roentgenogram one year after closure of defect, showing slight increase in heart size with continued inconspicuous vascular markings.

5. *Large Defect with Right-to-Left Shunt.* In this group there is severe pulmonary hypertension and a predominant right-to-left shunt and the heart is usually small without ventricular dilatation. The right ventricle is hypertrophied, as demonstrated by elevation of the apex in the posteroanterior projection and increased convexity in the left anterior oblique view (Fig. 5). The aorta is small, but the main pulmonary artery segment is extremely prominent. The vascular markings in each hilus are also

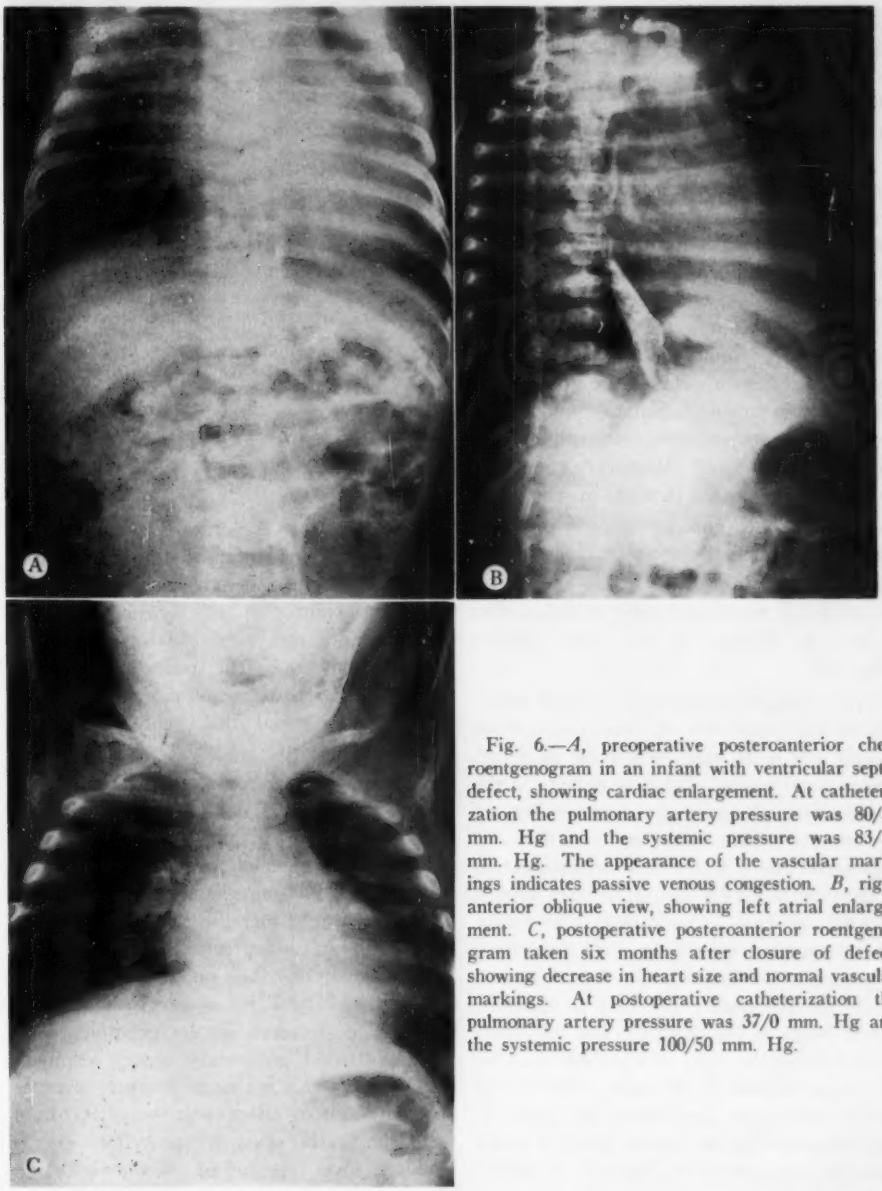


Fig. 6.—*A*, preoperative posteroanterior chest roentgenogram in an infant with ventricular septal defect, showing cardiac enlargement. At catheterization the pulmonary artery pressure was 80/38 mm. Hg and the systemic pressure was 83/50 mm. Hg. The appearance of the vascular markings indicates passive venous congestion. *B*, right anterior oblique view, showing left atrial enlargement. *C*, postoperative posteroanterior roentgenogram taken six months after closure of defect, showing decrease in heart size and normal vascular markings. At postoperative catheterization the pulmonary artery pressure was 37/0 mm. Hg and the systemic pressure 100/50 mm. Hg.

accentuated but become markedly narrowed and inconspicuous in the mid and peripheral portions of the lungs. The left atrium is not enlarged. An occasional case may be encountered in which the radiographic features appear essentially normal, the heart being of normal size and the right ventricular enlargement not apparent. In such cases the clinical findings, electrocardiographic data, and information gained from catheterization serve to indicate the correct classification.

The radiographic features of large ventricular septal defects in infants (Fig. 5) are usually not characteristic. The condition has not been present for a significant length of time to produce the chamber enlargement seen in older children, and in addition the thymus obscures the configuration of the superior portion of the heart. The cardiac enlargement appears more generalized, and selective chamber dilatation and hypertrophy are more accurately determined electrocardiographically. However, in large defects at this age the increase in pulmonary vascularity and enlargement of the left atrium are usually obvious radiologic features. In addition, the correlation of radiographic features and catheterization data is not as accurate as in older children (Fig. 6).

Venous angiocardiography plays a minor role in the evaluation of ventricular septal defects and is of much less value than cardiac catheterization. Dilution defects in the opacification of the right ventricle by the left-to-right shunt may be identified by angiocardiograms [3] as well as reopacification of the right ventricle and pulmonary vessels after filling of the left ventricle. Otherwise, the information gained by such procedure is generally not helpful. In those cases in which the pulmonary pressure is approximately equal to the systemic and the shunt is predominantly right to left there may be early opacification of the aorta. This is not always reliable, as exemplified in Figure 7. The angiocardiogram shown here is taken from the case shown in Figure 5, in which

Fig. 7.—Angiocardiogram of patient with severe pulmonary hypertension (Fig. 5), showing opacification of right auricle, right ventricle, and pulmonary artery. Early opacification of aorta did not occur. Although the intracardiac shunt was predominantly right to left in this patient; this feature was not demonstrable by angiocardiography.

the shunt was known to be predominantly right to left but premature opacification of the aorta did not occur. Of more value, particularly in differentiating ventricular septal defects from extracardiac shunts, is retrograde aortography.[4] By this procedure, in which contrast material is injected retrogradely into the brachial artery, the absence of opacification of the pulmonary vessels is presumptive proof that ventricular septal defect is present.

Changes in size and configuration of the heart and in pulmonary vascularity following surgical closure of ventricular septal defects develop slowly over a period of several months. Immediately after surgery there is a slight increase in heart size, usually with an unappreciable change in the prominence of the pulmonary vascular markings. There is, however, usually an immediate decrease in the prominence of the undivided pulmonary artery segment, but whether this is due to pressure changes or the result of changes in the pericardium incident to the operative procedure is unknown. Over a period of several weeks and

often months there is a gradual decrease in the size of the heart and in the prominence of pulmonary vascular pattern.

Summary

The radiologic features of isolated ventricular septal defects are discussed. A classification is presented based upon a correlation between the radiologic findings and the pressure relationships and intracardiac shunts determined at cardiac catheterization. This classification was applied in selection of 150 patients for repair of ventricular septal defects in using open-heart techniques.

1200 M. D. Anderson Blvd. (25) (Dr. Cooley).

REFERENCES

1. McNamara, D. G.; Cooley, D. A.; Latson, J. R.; Beard, E. F., and Singleton, E. B.: Ventricular Septal Defects: Evaluation of 300 Patients Including 150 Surgically Treated Cases, presented at the Third World Congress of Cardiology, Brussels, Belgium, September, 1958.

2. Cooley, D. A.; Latson, J. R., and Keats, A. S.: Surgical Considerations in Repair of Ventricular and Atrial Septal Defects Utilizing Cardiopulmonary Bypass: Experience with 104 Cases, Surgery 43:214-225 (Feb.) 1958.

3. Figley, M. M.; Nordenström, B.; Stern, A. M., and Sloan, H.: Angiocardiographic Mixing Defects as Indicators of Left to Right Shunts, Acta radiol. 45:425-437 (June) 1956.

4. Singleton, E. B.; McNamara, D. G., and Cooley, D. A.: Retrograde Aortography in the Diagnosis of Congenital Heart Disease in Infants, J. Pediat. 47:720-726 (Dec.) 1955.

Sarcoma of the Urachus

DONALD B. BUTLER, M.D., and HARVEY S. ROSENBERG, M.D., Houston, Texas

The urachus is a vestigial remnant of embryonic life. It extends from the apex of the bladder toward the umbilicus. In the fetus the urachus is a hollow tube which attaches the bladder to the allantoic stalk. At birth the urachus descends with the bladder and comes to lie in the midline directly over the apex of the bladder. The two umbilical arteries become obliterated and are drawn together and drawn down in the midline, forming a continuous band, the ligamentum commune, which passes from the umbilicus to the apex of the urachus. In adult life the urachus extends from the apex of the bladder to a point approximately one-third of the distance to the umbilicus, and above this point the ligamentum commune continues as a midline structure.

The urachus is occasionally the source of neoplastic disease. It is lined with transitional epithelium and may give rise to carcinoma. The surrounding wall may produce tumors of mesenchymal origin.

Shaw [7] in 1949 reviewed the subject of sarcoma of the urachus extensively and studied all of the reported cases in the literature at that time. He suggested three basic criteria which he felt were necessary before a tumor could be accepted as a sarcoma of urachal origin:

1. The tumor must occupy a site consistent with the anatomical position of the urachus at the age of the patient.
2. There should be a demonstrable anatomical relationship between the tumor and the urachus.
3. The tumor must possess the pathological and histological features of a sarcoma.

Submitted for publication, May 18, 1959.

Department of Surgery, Baylor University College of Medicine (Dr. Butler); Department of Pathology, Texas Children's Hospital (Dr. Rosenberg).

Shaw carefully studied the reported cases and it was his feeling that there was no completely substantiated case of sarcoma of the urachus at that time. He reviewed the reports of six patients with tumors of urachal origin that had been collected by Begg [1] and concluded that three of these cases should be rejected and the other three were possible urachal sarcomas.

Shaw reported in detail a case which he felt fulfilled the criteria for diagnosis of urachal sarcoma. This was a 6½-year-old boy admitted with an initial diagnosis of acute appendicitis. A large tumor was found involving the anterior abdominal wall and extending into the peritoneal cavity and attached to the omentum. The tumor was diagnosed as a spindle-cell sarcoma. The child had deep x-ray therapy but was readmitted with a large, recurrent mass and died seven months after the onset of symptoms.

The six cases which Shaw reviewed in 1949 (Table) as possible urachal sarcomas constitute the entire literature on the subject. There have been no subsequent cases reported.

Report of a Case

A 6-year-old Negro boy was seen in consultation on March 15, 1957, with a history of abdominal pain of 36 hours' duration. The child had been given castor oil without relief. The pain had localized in the right lower quadrant in the past six hours. The child had vomited and had one liquid bowel movement.

Past history was noncontributory. The child had had no previous surgery and no previous serious illnesses and had never been hospitalized.

Examination revealed a well-developed 6-year-old Negro boy who was acutely ill and quite toxic. His pulse was 100 per minute, and his temperature was 101.2 F rectally. Respirations were rapid, and the child was semistuporous. Abdominal examination revealed moderate distention with marked rigidity over the entire lower abdomen. There was marked tenderness in the right lower

Sarcoma of the Urachus: Collected Cases

Author	Date	Sex	Age	Clinical Picture	Pathological Features		Treatment	Course
					Gross	Diagnosis		
Frank [8]	1893	M	11 yr.	Anorexia, weight loss, abdominal mass	Tumor involved recti and vertex of bladder; nodules in omentum	Spindle-cell sarcoma	Excised	--
Fulle [4]	1913	M	40 yr.	Abdominal mass	Adherent to bladder, urachus, obliterated umbilical arteries present; nodules in peritoneum	Round and spindle-cell sarcoma	Biopsy	Died—3 mo.
Greig [5]	1927	F	30 yr.	Abdominal mass	No attachment to umbilicus; attached to bladder by delicate strand	Small-cell sarcoma	Excised	Living and well 7 yr. later
Voncken & Cambresier [3]	1927	F	30 yr.	Abdominal mass	Attached to posterior rectal sheath	Fibrosarcoma	Excised	--
Ransom [6]	1933	F	4 mo.	Abdominal mass	Attached to anterior abdominal wall, umbilicus to bladder; 11.5 cm. in diameter	Spindle-cell rhabdomyosarcoma	Excised en bloc	Living and well 2 yr. later
Shaw [7]	1949	M	6 yr.	Abdominal pain, fever, tenderness	Bloody ascites, projecting into peritoneal cavity, attached to omentum	Spindle-cell sarcoma	Excised en bloc with omentum irradiation	Died—7 mo.
Butler and Rosenberg	1959	M	6 yr.	Abdominal pain, fever, tenderness, leukocytosis	12 cm. in diameter, bloody ascites, adherent to omentum; attached to umbilicus and bladder by cord-like structure	Sarcoma	(1) Excised en bloc with omentum; (2) irradiation; (3) actinomycin D; (4) mechlorethamine hydrochloride	Died—3 mo.

quadrant. Rectal examination revealed marked tenderness but no definite mass.

Laboratory examination revealed a hemoglobin of 11.7 gm., a hematocrit of 35%, a leukocyte count of 14,800 with a slight left shift. The child was admitted to Texas Children's Hospital with a presumptive diagnosis of acute appendicitis with generalized peritonitis and probable appendiceal abscess.

The patient was taken to surgery immediately. After induction of anesthesia it was obvious that there was a mass involving the lower abdomen, and the patient was catheterized, but the mass persisted. It was our impression that this probably represented an appendiceal abscess. The abdomen was opened through a right transverse incision, and when the peritoneal cavity was opened a moderately large amount of bloody, ascitic fluid was evacuated. Exploration revealed a large tumor involving the anterior abdominal wall in the midline.

The incision was extended as a transverse incision across both recti just below the umbilicus. A cord-like attachment of the tumor to the umbilicus was noted, and this was carefully dissected free and not transected. The lower flap of the abdominal wall was mobilized widely, and the large tumor mass, which was approximately 12 cm. in diameter, was readily mobilized. The greater omentum was adherent to the left side of the mass and on the right side the mesentery of the terminal ileum and cecum was loosely adherent to the mass. Both structures were freed easily with blunt dissection. The tumor was then removed quite easily, having a good plane of cleavage and it was noted that the right obliterated umbilical artery extended into the tumor just at its upper border. Upon further dissection it was apparent

Fig. 1.—Urachal tumor showing attachment to bladder. Note ligamentum commune has been transected from umbilicus.

that the tumor was attached to the bladder by a midline tubular structure approximately 0.25 cm. in diameter and 4 cm. in length (Fig. 1). The tumor and the tubular remnants were resected. The bladder defect was closed in layers. The greater omentum was resected as it was felt that it was probably involved with the tumor.

Pathologic Examination.—The tumor consisted of a multilobulated gray and red structure measuring 10.0 by 9.0 by 4.0 cm. and weighed 186 gm. The umbilical and bladder ends of the specimen were identified by a cylindrical and a cystic area respectively. On cut section, the structure was firm, white, and unencapsulated. There were large mucoid, somewhat gelatinous areas. A moderate degree of vascularity was observed throughout the specimen.

Microscopically, there was a dense fibrous capsule which was poorly respected as a boundary by a densely cellular neoplasm. The tumor was made

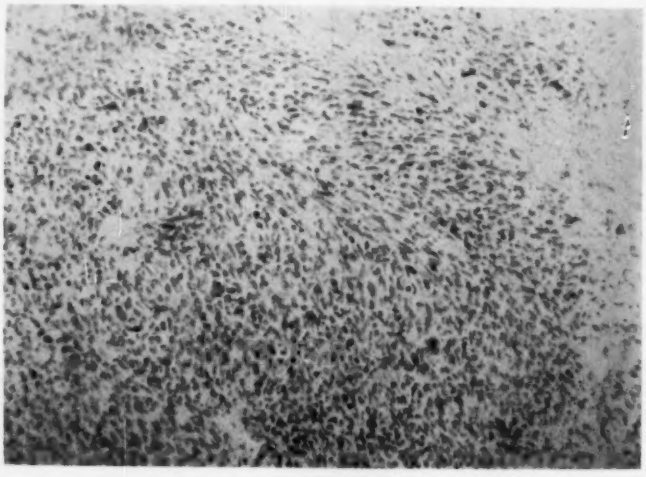


Fig. 2.—Urachal sarcoma. Typical microscopic picture.

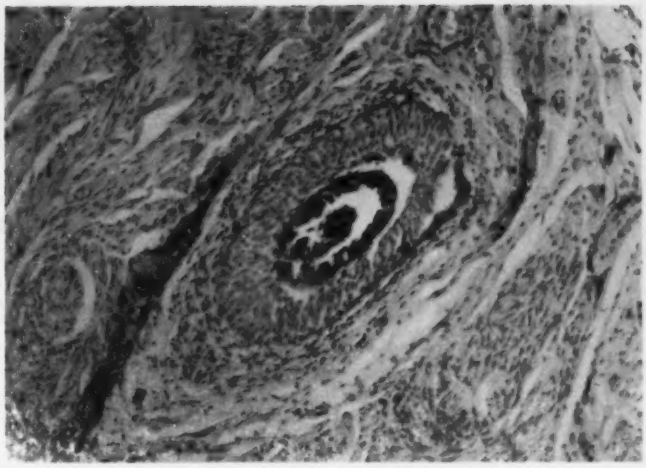


Fig. 3. — Microscopic section through urachal remnant showing duct lined by transitional epithelium.

up of broad sheets of irregularly interlacing tissue. Multiple areas of fresh hemorrhage and necrosis were encountered. Cytologically, there was a moderate variation in cell type ranging from plump, round forms to elongated spindle-shaped cells. A few large bizarre multinucleated forms were also encountered. Occasional elements were encountered in which there was a large, round nucleus and a long streamer of cytoplasm. The cytoplasm was finely granular in some forms and poorly defined in others. Striations were not encountered despite prolonged search in hematoxylin and eosin and phosphotungstic acid hematoxylin preparations (Fig. 2).

In the area which was grossly identified as urachus, there was a thin, patent canal lined by transitional-type epithelium and surrounded by smooth muscle in an orderly pattern (Fig. 3). At the point at which the urachus entered the neoplasm, no epithelial component could be identified. Only undifferentiated neoplastic tissue was encountered at this point.

The pathologic interpretation was that of a soft tissue sarcoma of the abdominal wall.

Postoperative Course.—The child recovered rapidly from surgery and was dismissed from the hospital on the 10th postoperative day. The child was referred to M. D. Anderson Hospital for chemotherapy and roentgen therapy. On April 16, 1957 (30 days postoperatively) abdominal examination revealed some distention and tenderness in the lower abdomen. By April 22 the tumor was obviously rapidly growing and extended 3 cm. above the umbilicus. The patient was given actinomycin D without effect upon the rapid growth of the tumor. On April 26, 1957, the tumor extended to the costal margin bilaterally. Mechlorethamine hydrochloride (nitrogen mustard) was given in full therapeutic dose also without any noticeable effect upon the tumor. The child rapidly became more distended and was unable to breathe except in a sitting position. Cachexia progressed, and on June 24, 1957, the child died. This was slightly more than three months after onset of symptoms.

Autopsy examination revealed a huge abdominal tumor weighing 3,840 gm. extending from costal margin to pelvis and involving the liver, kidneys, and diaphragmatic muscle.

Comment

The striking similarity of the above case to that case described by Shaw in 1949 is apparent. In both cases a 6-year-old boy was admitted with a presumptive diagnosis of acute appendicitis. In both cases a urachal tumor was found involving intraperitoneal structures by direct extension. In both cases resection of the tumor was performed without any difficulty and rapid recurrence and death followed.

The history of abdominal pain prior to the discovery of the abdominal tumor is undoubtedly related to the rapid growth of the tumor, with some hemorrhage into the peritoneal cavity occurring as the tumor extended into the omentum. It is doubtful whether en bloc resection of the entire lower abdominal wall would have offered any greater chance of cure in the present case. The refractoriness of this tumor to certain of the chemotherapeutic agents used in can-

cer therapy is not unusual for sarcomas of this type.

1509 Medical Towers Building.

REFERENCES

1. Begg, C.: Colloid Adenocarcinomata of the Bladder Vault Arising from the Epithelium of the Urachal Canal, with a Critical Survey of the Tumours of the Urachus, Brit. J. Surg. 18:422-466, 1931.

2. Voncken and Cambresier: Tumeurs solides de ouraque, Arch. méd. belges 80:420-422, 1927.

3. Frank, T.: Zur Kasuistik der Urachus Tumorn, Inaugural Dissertation, Wurzburg, 1893.

4. Fulle, G. B. C.: Sarcoma polimorfo primitivo dell uraco, Gazz, Internat. med. 17:37-40, 1913.

5. Greig, D. M.: Report of a Case of Sarcoma of the Urachus, Edinburgh M. J. 34:425-426, 1927.

6. Ransom, H. C.: Sarcoma of the Urachus: Review of the Literature with Report of an Additional Case, Am. J. Surg. 22:187-191, 1933.

7. Shaw, R. E.: Sarcoma of the Urachus: Report of a Case and Brief Review of the Subject, Brit. J. Surg. 37:95-98, 1949.

Effect of Intravenous Heparin on Terminal Temperature in the Hypothermic Dog

LEONARD CARANNA, M.S.; VERNON MONTGOMERY, M.D., Ph.D., and HENRY SWAN, M.D., D.Sc., Denver

The terminal temperature of surface-cooled adult dogs is remarkably constant. If we define the terminal temperature as the rectal temperature at which a dog's heart succumbs either to ventricular fibrillation or to cardiac arrest, we find from the literature the following mean terminal temperatures: 16.5 C, DeBoer et al.[1]; 18.5 C, Covino et al.[2]; 18.6 C, Hegnauer,[3] and in the present no-treatment group, 19.4 C. Young dogs withstand much lower temperatures. DeBoer [1] found that the mean lethal temperature of young dogs was 9.5 C. The present paper describes experiments in which the mean terminal temperature of adult surface-cooled dogs was significantly reduced below those values reported above.

Caranna et al.[4] have shown that survival of animals cooled to 25 C and subjected to intracardiac surgery is increased by the infusion of nutrients; therefore, we wished to determine whether a continuous infusion of 5% dextrose would decrease the mean terminal temperature in dogs. Willson and Eliot [5] have shown there is intravascular sludging of formed elements in the blood of dogs cooled to 25 C. Ellis et al.[6] have shown that microscopic sections of lung tissue of animals cooled to 24 to 29 C reveal complete occlusion of small pulmonary vessels by thrombi. The latter workers showed further that intravenous heparin, given during the period of cooling, prevented these phenomona. Therefore, we also wished to determine whether an administration of intravenous heparin during the cooling period would reduce the mean terminal temperature. And, finally, we wished to determine whether a vasopresser agent might be of benefit to animals being subjected to profound hypothermia by inducing a more active circulation. Phenylephrine (Neo-Synephrine) hydrochloride was chosen as the vasopressor agent, since it has been shown that this monohydroxycatacholamine has only slight fibrillatory effect.[7,8]

Methods

Sixty-nine apparently healthy mongrel dogs, ranging in weights from 7.2 to 21.5 kg., were used in this study. Prior to an experiment, the age of each animal was estimated from observation of the teeth.[9] The teeth age of these animals ranged from 1½ to 8 years. This method of estimating the age of an animal no doubt is a crude one, but we feel it serves as a useful guide. All animals were deeply anesthetized with approximately 35 mg/kg. of pentobarbital (Nembutal). An endotracheal tube was inserted, and the animal was artificially ventilated throughout the period of observation. Polyethylene catheters were inserted into the right femoral artery and vein for continuous monitoring of femoral arterial pressure and infusion of fluids via the vein. Arterial pressures were transmitted to an unbonded strain gauge and amplified and recorded on a multichannel oscilloscope-type recorder. Lead II of the electrocardiogram was monitored continuously on an oscilloscope. The rectal temperatures were determined by means of a chemical thermometer inserted about 6 or 7 cm. into the rectum. After the institution of artificial respiration and the placement of catheters, the animal was placed in an ice bath with the limbs and head out of the water. If fluids were being administered during the period of cooling, the intravenous infusion was

Submitted for publication April 27, 1959.

From the Halsted Laboratory of Experimental Surgery, University of Colorado School of Medicine.

Dr. Montgomery's work was done during the tenure of an Advanced Research Fellowship of the American Heart Association.

This study was aided in part by a grant from the U.S. Public Health Service (H-2710) and in part by a grant from the Colorado Heart Association.

begun immediately after placing the animal in the ice bath. The infusion was administered through the femoral vein catheter.

Observations were recorded at normothermia, at 30 C, 25 C, 20 C and the terminal rectal temperature. If the animal succumbed to ventricular fibrillation, the temperature at which this event occurred was recorded. Because of the very slow heart rate, it is very difficult to determine when an animal in profound hypothermia is truly in cardiac arrest, even though arterial pressures and EKG are being monitored. Therefore, we have arbitrarily defined cardiac arrest in our experiments as no detectable cardiac event occurring within twice the previously detected rate. For example, if the previous detected rate was one beat per 10 minutes, then 20 minutes of continuous observation without a cardiac event was called cardiac arrest.

The animals of these experiments were divided into seven series as follows:

Series I (11 Dogs).—No treatment was given throughout the entire period of cooling.

Series II (10 Dogs).—These animals received a continuous infusion of 5% mannitol in isotonic saline at a rate of 0.3 ml/kg/min. This group served as a control to the osmotic effect of the 5% dextrose and saline.

Series III (10 Dogs).—These animals received continuous infusions of 5% dextrose in isotonic saline. The rate of infusion was approximately 0.3 ml/kg/min.

Series IV (10 Dogs).—These animals received no therapy other than a total dose of 6 mg/kg. of heparin administered intravenously. This total dose of heparin was divided into three equal parts, 2 mg/kg. being given at a normal temperature, 30 and 20 C. This method of administration of heparin was used in all series receiving heparin.

Series V (10 Dogs).—Animals of this group received a continuous infusion of 5% dextrose as in Series III. In addition, these animals received heparin as described in Series IV.

Series VI (8 Dogs).—Animals of this group received a continuous infusion of 5% dextrose in isotonic saline and phenylephrine. The rate of dextrose infusion was the same as in Series III. The rate of phenylephrine infusion was 0.06 mg/min.

Series VII (10 Dogs).—These animals received the same treatment as those of Series VI plus 6 mg/kg. of heparin.

Results

The mean terminal temperature of each animal is listed in the Table. The animals are grouped according to their treatment series. The asterisks beside a temperature indicate that the terminal event was cardiac standstill. The means and S.E. of the means of each series are listed under their respective series. Two *P* values are listed. The first row of *P* values was obtained by Fisher's *t* test for the significance of the difference between means of Series I and each of the other series. This analysis

Summary of Data

I	II	III	IV	V	VI	VII
No Treatment	Mannitol	Dextrose	Heparin	Heparin and Dextrose	Phenylephrine and Dextrose	Phenylephrine, Dextrose and Heparin
Temp., C	Temp., C	Temp., C	Temp., C	Temp., C	Temp., C	Temp., C
15.0	22.0	21.0	9.3 *	17.8	18.0	20.5
18.0 *	16.0 *	14.0 *	14.7	9.1 *	10.0 *	10.0 *
22.0	20.5	20.0	14.5	11.0	19.0	11.8
17.0 *	20.0	17.0 *	13.5 *	10.5 *	16.5	9.0 *
22.0	19.5	22.0	18.8	12.1	16.6	12.0
20.0 *	15.0	21.0 *	13.5	13.5	16.5	10.5 *
22.5	20.0	20.0	14.0 *	9.5	18.5	15.0
20.0 *	18.5	12.5	15.0	9.8 *	19.0	9.4 *
24.0	19.5	20.0 *	18.0	11.4 *		11.5
16.5 *	22.0	17.8	16.0 *	16.4		13.0
16.5 *						
Mean 19.4	19.3	18.5	14.7	12.1	16.8	12.3
S. E. 0.90	0.72	1.00	0.83	0.93	1.04	1.07
P	0.50	0.50	0.001	0.001	0.05-.10	0.001
† *P*				0.05	0.10-.20	0.05-0.10

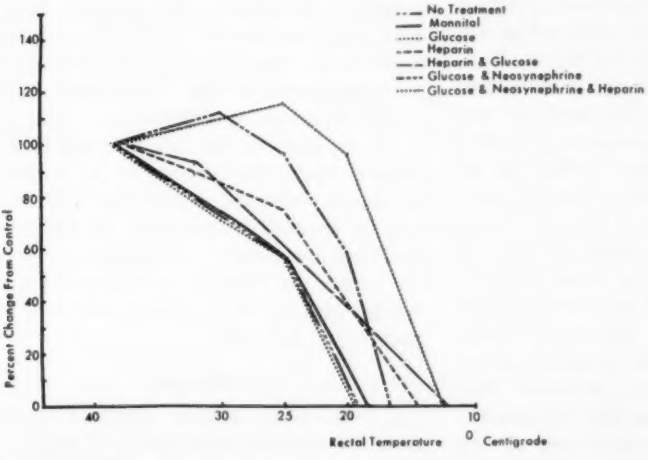
* Indicates cardiac standstill; remainder represent ventricular fibrillation.
P Determined by Fisher's *t* test. All series (II, III, IV, V, VI, VII) were tested against Series I.
† *P* Series V, VI, and VII tested against Series IV.

clearly demonstrates two points. The administration of either 5% dextrose or mannitol in normal saline alone has little or no influence on the mean terminal temperature of adult surface-cooled dogs. Note, however, that the *P* values of Series IV, V, and VII are highly significant. You will note further that heparin was administered in each of these series and only in these series. These observations point emphatically to one conclusion: Heparin administration significantly reduced the mean terminal temperature of these animals.

The intermediate position of the mean and *P* value of Series VI permits no such definite statement as to the influence of the combined treatment with phenylephrine and dextrose. The second row of *P* values tests the significance of the differences between the means of Series IV, on the one hand, and Series V, VI, and VII, on the other. Note that the *P* values for Series V and VII are statistically significant and that the means of these two groups are not different from each other. In other words, the addition of heparin treatment (Series VII) to the combined phenylephrine and dextrose treatment (Series VI) significantly lowered the mean terminal temperature. Yet, removal of phenylephrine (Series V) from the combined treatment of phenylephrine, dextrose, and heparin (Series VII) did not alter the mean terminal temperature. Therefore, we are led to the conclusion that phenylephrine did not significantly influence the mean terminal temperature in these experiments.

Earlier we stated there was no evidence in these experiments that dextrose treatment alone influenced the mean terminal temperature. Now we must make a more difficult decision: Does the presence or absence of dextrose treatment influence heparin treatment? The Table shows the mean terminal temperature with heparin treatment alone (Series IV) was 14.7. When dextrose was added to the heparin treatment (Series V), the mean terminal temperature was 12.1 C. However, these differences are not statistically significant ($P=0.05$). We can only say that there are about 5 chances in 100 that dextrose treatment with heparin lowers the terminal temperature below that attainable by heparin alone. The lack of significance may be due to the inadequate sample sizes. Series VII has a mean of 12.3, which again is lower than the mean terminal temperature with heparin alone, but the means are not statistically signficant.

Statistical comparison of the incidence of ventricular fibrillation with the incidence of cardiac standstill with any given treatment was negative.



The per cent change in blood pressure from the normothermic level. The ordinate equals per cent change from control (100%). The abscissa equals rectal temperature, Centigrade.

The Figure illustrates the change in mean arterial pressure of each series as cooling progresses. The pressures are plotted as a per cent of the series mean, mean arterial pressure. Note that the pressure changes of Series I, II, and III were almost identical and were always lower than the other series. Yet, the maintenance of mean arterial pressure is not clearly related to the mean terminal temperature. Down to 20 C the two series receiving phenylephrine (Series VI and VII) had the highest pressures, but absence of heparin in Series VI still resulted in a mean terminal temperature no different from Series I, II, and III. Series V, which had the lowest mean terminal temperature, had an intermediate mean arterial pressure.

The heart rate changes were similar in all series.

Comment

We have defined the terminal temperature as that rectal temperature to which an animal can be cooled by surface cooling before the advent of ventricular fibrillation or cardiac arrest. The present work shows that the terminal temperature of dogs can be significantly lowered by the administration of heparin. It should be emphasized here that the dose of heparin used in these experiments is extremely high—6 mg/kg. In addition, it should be noted this dose was divided into three injections: 2 mg/kg. was administered as soon as the animal was placed in the ice bath, 2 mg/kg. at 30 C, and 2 mg/kg. at 20 C. We have not altered this routine; therefore, we have no idea what the minimum requirements of heparin are to produce this effect. Neither do we know that multiple injections are necessary.

There are at least three separate properties of heparin which could account for its ability to reduce the terminal temperature of dogs. Ellis et al.[6] have demonstrated microthrombi of small pulmonary vessels in animals cooled to 24-29 C and found the administration of heparin prevented their occurrence. It is possible that heparin has lowered the terminal temperatures of our animals by the prevention of such a process. Willson and Eliot[5] have observed intravascular agglutination of erythrocytes, sticking of white cells to venule walls, and apparent hemoconcentration in animals cooled to 25 C. Knisely et al.[10] demonstrated that heparin prevents sludging in other conditions, and this effect may have been important in the experiments of the present report. Finally, it is known that heparin clears plasma of chylomicrons in vitro and in vivo. It is possible that chylomicrons may grow, at low temperatures, to the point of causing small fat emboli throughout the body. Caranna et al.[4] reported that all animals receiving intravenous Lipomul (a vegetable oil emulsion), while being cooled to 25 C, died. At autopsy these animals were found to have massive fat embolized areas in the lungs. It is not possible, with the present information, to decide which, if any, of the above effects of heparin is responsible for its terminal temperature reducing effect.

It is interesting to note that dextrose treatment alone has no effect on the terminal temperature of dogs but, in conjunction with heparin, dextrose reduces the terminal temperature below that achieved with heparin alone. The mechanism of action of dextrose in this instance is unknown. It is known that cooling to 25 C causes a moderate hypoglycemia which tends to progress with time.[11] It is possible, therefore, that the slowly produced profound hypothermia reported here also produces a profound hypoglycemia. At present, however, this is mere speculation.

On the basis of the data obtained in the present report, there seems to be no relationship between the arterial blood pressure and the terminal temperature. In addition, phenylephrine-induced hypertension does not reduce the terminal temperature below that achieved by the combined treatment of glucose and heparin.

Conclusions

1. Intravenous heparin significantly reduces the terminal temperature of dogs.

2. Continuous infusion of 5% dextrose in isotonic saline potentiates the terminal temperature reducing effect of heparin.

4200 E. 9th Ave. (20) (Dr. Swan).

REFERENCES

1. DeBoer, B., and Ederstrom, H. E.: Lethal Hypothermia in Dogs of Various Ages, Anesthesiology 7:518-521, 1946.

2. Covino, B. G.; Charleson, D. A., and D'Amato, H. E.: Ventricular Fibrillation in the Hypothermic Dog, Am. J. Physiol. 178:148-154, 1954.

3. Hegnauer, A. H.; Flynn, J., and D'Amato, H.: Cardiac Physiology in Dog During Rewarming from Deep Hypothermia, Am. J. Physiol. 167:69-75, 1951.

4. Caranna, L. J.; Telmosse, F. J. P., and Swan, H.: Effect of Intravenous Nutrient Solutions on Ventricular Fibrillation in the Hypothermic Dog, A.M.A. Arch. Surg. 76:394-397, 1958.

5. Willson, J. T.; Miller, W. R., and Eliot, T. S.: Blood Studies in the Hypothermic Dog, Surgery 43:979-989, 1958.

6. Ellis, P. R.; Kleinsasser, L. J., and Speer, R. J.: Changes in Coagulation Occurring in Dogs During Hypothermia and Cardiac Surgery, Surgery 41:198-209, 1957.

7. Swan, H., and Montgomery, A. V.: Pharmacology of the Heart, in Extracorporeal Circulation, Springfield, Ill., Charles C Thomas, Publisher, 1958, pp. 433-450.

8. Meek, W. J.: Some Cardiac Effects of the Inhalant Anesthetics and the Sympathomimetic Amines, Harvey Lect. 36:188-227, 1941.

9. Boenisch, F.: Beitrag zur Altersbestimmung des Hundes nach den Schneidezähnen, Arch. wissensch. u. prakt. Tierh. 39:289-327, 1912-1913.

10. Knisely, M. H.; Stratman-Thomas, W. K.; Eliot, T. S., and Bloch, E. H.: Knowlesi Malaria in Monkeys: II. A First Step in Separation of Mechanical Pathologic Circulatory Factors of One Sludge Disease from Possible Specific Toxic Factors of that Disease, Anat. Rec. 109:53, 1951.

11. Holmes, J. H.; Montgomery, A. V.; Zeavin, I.; Prevedel, A. E., and Swan, H.: Metabolic Changes in Hypothermia, J. Lab. & Clin. Med 42:816, 1953.

Use of Cardiotonic Agent (Mephentermine) in Myocardial Depression Due to Potassium

THEODORE COOPER, M.D., Ph.D., Bethesda, Md.; VALLEE L. WILLMAN, M.D.; PANAGIOTIS ZAFIRACOPOULOS, M.D., and C. ROLLINS HANLON, M.D., St. Louis

Recent studies have demonstrated that prolonged induced cardiac arrest is followed by myocardial damage [1,2] and depressed ventricular function [3] in the dog. It has also been shown that this depression may be limited by prophylactic digitalization [4] and by hypothermia.[5] The present communication reports our experiences with the use of mephentermine sulfate (Wyamine), a cardiotonic and pressor agent,[6] in dogs in which myocardial function has been depressed by a 30-minute period of asystole induced by potassium citrate.

Methods

Mongrel dogs of 8.5 to 12.5 kg. body weight were used. Anesthesia was induced by intravenous thiopental sodium. Complete respiratory paralysis was obtained with intravenously administered succinylcholine. The animals were respired [7] with 100% oxygen at pressures of 15 to 20 cm. water. Esophageal temperature was recorded by a thermistor probe.

Femoral arterial pressure was measured by means of a P23A Statham transducer. Arterial blood was sampled by way of an indwelling catheter in the carotid artery. A jugular vein was catheterized to permit rapid transfusion. After right thoracotomy, a small catheter of known capacity was inserted into the right atrium by way of the azygos vein as a conduit for rapid injection of dye. The left atrium was catheterized by way of a pulmonary vein for recording left atrial pressure by means of a water manometer. Cardiac output was measured by the indicator-dilution technique utilizing indocyanine green dye [8] and a cuvette densitometer.

Arterial pressures and Lead II of the electrocardiogram were recorded on a direct writing oscillograph. Indicator dilution curves were recorded on a direct writing milliammeter.

Ventricular function curves [9] were constructed by plotting calculated stroke work at various filling pressures (mean left atrial pressure) in response to transfusion of whole blood. Left ventricular stroke work in grammeters was calculated from the formula given at the bottom of the page.

Peripheral resistance was calculated according to the method of Green et al.[10]

After obtaining the necessary measurements for construction of a control left ventricular function curve, the right atrium and a femoral artery were cannulated, heparin, 2.4 mg/kg. was given intravenously, and cardiopulmonary bypass was instituted utilizing a rotating disc oxygenator. Mean arterial pressure was maintained at 100 mm. Hg. during the period of perfusion. Cardioplegia was induced with 2.5% potassium citrate in whole blood. The left heart was decompressed during the period of arrest to prevent cardiac overdistention, pulmonary engorgement,[11] and the effects of potassium ion accumulation.[1]

After 30 minutes of arrest, coronary perfusion was resumed. Ventricular defibrillation when necessary was accomplished with electroshock. Cardiac action was regularly resumed in less than 5 minutes. Ten to thirty minutes after the animal was able to support his circulation without aid from the pump oxygenator circuit, ventricular function was restudied.

Immediately after this baseline determination of cardiac function after arrest, mephentermine sulfate (0.5 mg/kg.) was given intravenously. Ventricular function was again assessed. In some animals, additional increments of the drug were given to investigate the possible benefits of repeated or larger doses.

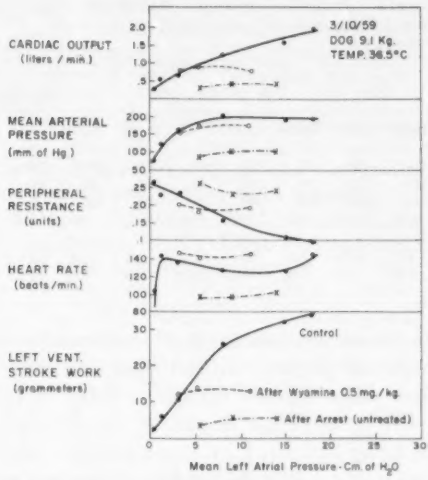
$$\text{Left ventricular stroke work} = \frac{\text{Stroke volume in cc.} \times (\text{mean arterial pressure in cm. } H_2O - \text{mean left atrial pressure in cm. } H_2O)}{100}$$

Submitted for publication May 21, 1959.

Aided by Grant H-3826 from the National Institutes of Health.

Mephentermine sulfate (Wyamine) supplied by Wyeth Laboratories, Philadelphia.

From the Department of Surgery, St. Louis University School of Medicine. National Heart Institute Trainee in Cardiovascular Surgery (Dr. Cooper). St. Louis Heart Association Fellow (Dr. Zafiracopoulos).



Graph illustrating the depressant effects of 30 minutes of asystole induced by potassium citrate and the improvement in function which followed the administration of mephentermine sulfate (Wyamine) 0.5 mg/kg. given intravenously.

Results

The graph demonstrates the pattern of response of one of six dogs subjected to 30 minutes of cardiac arrest and to the subsequent administration of mephentermine. Cardiac output, mean arterial blood pressure, heart rate and stroke work are depressed at all filling pressures following arrest. Calculated peripheral resistance is increased. Following the administration of 0.5 mg/kg. mephentermine sulfate intravenously, there is elevation of cardiac output, mean arterial pressure, heart rate, and stroke work over a similar range of filling pressures. Peripheral resistance fell. Previous studies have emphasized the fact that surgical manipulations and extracorporeal circulation of themselves do not cause depression in ventricular function.

Table 1 summarizes the cardiac output, blood pressure, stroke work, and minimum peripheral resistances in response to transfusion in the six animals before and after 30 minutes of elective potassium cardioplegia and after treatment with mephentermine sulfate (0.5 mg/kg.).

TABLE 1.—*Response of Dogs to Transfusion Before and After 30 Minutes of Cardiac Arrest Induced with Potassium Citrate and After Treatment with Mephentermine Sulfate (0.5 Mg/Kg.)*

		Control				After Arrest				After Mephentermine Sulfate			
Dog No.	Wt., Kg.	Max. CO, Cc/Min.	Max. MAP, Mm. Hg.	Max. LV8W, Grammeters	Min. PR, Units	Max. CO, Cc/Min.	Max. MAP, Mm. Hg.	Max. LV8W, Grammeters	Min. PR, Units	Max. CO, Cc/Min.	Max. MAP, Mm. Hg.	Max. LV8W, Grammeters	Min. PR, Units
2-3	9.0	2180	180	32.3	0.085	620	120	4.9	0.18	930	175	11.3	0.18
3-10	9.1	2000	200	34.3	0.088	412	100	5.1	0.24	960	175	13.7	0.19
3-13	8.5	2050	185	31.9	0.083	745	120	9.7	0.17	1530	180	29.8	0.12
3-20	11.3	2340	152	40.0	0.070	800	62	2.5	0.20	1040	150	10.7	0.14
3-23	10.4	2050	152	32.5	0.073	225	65	1.0	0.25	525	85	3.4	0.16
3-25	12.5	2700	170	35.5	0.058	465	90	2.6	0.13	820	110	5.2	0.12

Max. CO= maximum cardiac output; Max. MAP=maximum mean arterial pressure; Max. LV8W=maximum left ventricular strike work; Min. PR=minimum peripheral resistance.

TABLE 2.—*Immediate Response of Dogs with Potassium-Induced Myocardial Depression to Mephentermine Sulfate (Wyamine) (0.5 Mg/Kg.) Given Intravenously*

Dog No.	2-3		3-10		3-13		3-20		3-23		3-25	
	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After
Heart rate/min.	192	192	102	146	110	120	216	200	168	168	186	226
Mean arterial pressure, mm. Hg	120	175	105	155	110	180	50	140	60	85	87	100
Cardiac output, cc/min.	620	930	405	790	745	1,530	800	1,040	225	410	225	425
Left atria lpressure, cm. H_2O	12.0	9.0	15.0	3.0	20.0	11.0	14.0	7.5	11.0	5.0	7.5	2.0
Left ventricular stroke work, grammeters	4.9	11.3	5.1	11.3	9.7	29.8	2.0	9.6	1.0	2.8	1.4	2.7
Peripheral resistance, units	0.18	0.18	0.24	0.20	0.15	0.12	0.06	0.13	0.25	0.20	0.37	0.22

The depressant effects of cardiac arrest are evident in each animal. Mitigation of this depression by mephentermine was achieved in each dog, as is demonstrated by the improvement in cardiac output, stroke work, and blood pressure.

Table 2 shows the immediate response of each animal to the injection of the agent. In every case, left atrial pressure was decreased, and there was an increase in arterial pressure, cardiac output, and stroke work. Heart rates were unchanged or increased in five of six animals. Peripheral resistance was unchanged or decreased in five of six animals.

Comment

These studies demonstrate that the functional myocardial depression which follows 30 minutes of elective arrest with potassium citrate in the dog may be immediately mitigated in part by the administration of mephentermine sulfate. This drug has been used as a vasopressor [12] and has recently been shown to produce its pressor effect by improvement in myocardial contractility.[6] It is said to increase myocardial efficiency when given in the presence of an elevated left atrial pressure with heart failure. A complete dose response curve was not determined in these experiments. However, three animals who were given larger doses of the drug showed further improvement in function. The administration of a cardiac glycoside (ouabain 0.033 mg/kg.) to these animals resulted in a further small increment in cardiac output, blood pressure, and stroke work. No dysrrhythmia was noted. It seems reasonable that mephentermine might be given as adjunct myocardial support while digitalis therapy is being instituted or while the degree of digitalization is being estimated in those patients who had received digitalis previous to the cardiac arrest.

We have not evaluated the action of this agent in prolonging the survival time when the period of use is extended. The beneficial effects of the agent, however, indicate the advisability of further trial, experimentally and clinically, in an attempt to decrease the morbidity and mortality which follows prolonged cardioplegia.

Summary and Conclusion

Mephentermine sulfate (Wyamine) was given to dogs with evidence of severe myocardial depression induced by elective cardiac arrest with potassium citrate. In doses of 0.5 mg/kg., this cardiotonic agent increased cardiac output, blood pressure, and stroke work. Peripheral resistance was decreased.

These studies indicate that mephentermine might be useful in the postoperative management of subjects who have undergone extended periods of cardiac arrest.

Clinic of Surgery, National Heart Institute.

REFERENCES

1. Helmsworth, J. A.; Kaplan, S.; Clark, L. C.; McAdam, A. J.; Matthews, S. C., and Edwards, F. K.: Myocardial Injury Associated with Asystole Induced with Potassium Citrate, Ann. Surg. 149: 200, 1959.

2. Reynolds, S. R. M.; Kirsch, M., and Bing, R. J.: Functioning Capillary Beds in the Beating, K-Cl Arrested and the K-Cl Arrested-Perfused Myocardium of the Dog, Circulation Res. 6:600, 1958.

3. Willman, V. L.; Cooper, T.; Zafiracopoulos, P., and Hanlon, C. R.: Depression of Ventricular Function Following Elective Cardiac Arrest with Potassium Citrate, Surgery, to be published.

4. Cooper, T.; Willman, V. L.; Zafiracopoulos, P., and Hanlon, C. R.: Effect of Prophylactic Digitalization on Myocardial Function After Elective Cardiac Arrest, Ann. Surg., to be published.

5. Cooper, T.; Willman, V. L.; Zafiracopoulos, P., and Hanlon, C. R.: Myocardial Function After Elective Cardiac Arrest During Hypothermia, Surg. Gynec. & Obst., to be published.

6. Welch, G. H., Jr.; Braunwald, E.; Case, R. B., and Sarnoff, S. J.: The Effect of Mephentermine Sulfate on Myocardial Oxygen Consumption, Myocardial Efficiency and Peripheral Vascular Resistance, Am. J. Med. 24:871, 1958.

7. Hanlon, C. R.; Johns, T. N. P., and Thomas, V.: An Apparatus for Anesthesia in Experimental Thoracic Surgery, J. Thoracic Surg. 19:887, 1950.

8. Hetzel, R. S.; Swan, H. J. C.; Ramirez de Arellano, A. A., and Wood, E. H.: Estimation of Cardiac Output from First Part of Arterial Dye Dilution Curves, J. Appl. Physiol. 13:92, 1958.

9. Sarnoff, S. J.: Myocardial Contractility as Described by Ventricular Function Curves: Observations on Starling's Law of the Heart, Physiol. Rev. 35:107, 1955.

10. Green, H. D.; Lewis, R. N.; Nickerson, N. D., and Haller, A. C.: Blood Flow, Peripheral Resistances and Vascular Tonus with Observations on Relationship Between Blood Flow and Cutaneous Temperatures, Am. J. Physiol. 141: 518, 1944.

11. Ross, J., Jr.; Gilbert, J. W., Jr.; Sharp, E. H., and Morrow, A. G.: Elective Cardiac Arrest During Total Body Perfusion: The Relationship of Elevated Intracardiac Pressures During Arrest to Subsequent Myocardial Function and Pathologic Pulmonary Changes, J. Thoracic Surg. 36:543, 1958.

12. Winsor, T.: Mephentermine Sulfate for Treatment of Arterial Hypotension, J.A.M.A. 169: 1742, 1959.

Primary Idiopathic Segmental Infarction of the Greater Omentum

Report of Four Cases and Review of Literature

EARL J. HALLIGAN, M.D., Jersey City, N. J., and FOUAD A. RABIAH, M.D., Highland Park, Mich.

Idiopathic omental infarction is one of the rare causes of acute abdomen which is usually not diagnosed preoperatively, but found unexpectedly on exploration of the abdomen. This disease, though rare, is important to the surgeon becauses it mimics the common causes of acute abdomen.

The first case of omental infarction was reported by Bush [6] in 1896. Other terms used to describe this clinical entity are acute segmental infarction, omental infarction, omental segmental infarction, spontaneous infarction of the greater omentum, hemorrhagic infarction of the greater omentum, thrombosis of the omentum, hemorrhage into the greater omentum, primary omental torsion, omental volvulus, acute epiploitis, etc. It is our opinion that the most correct term for this disease is "primary idiopathic segmental infarction of the greater omentum."

Wrizeresinski et al.[43] postulated the following criteria which are required for every case:

1. The infarction of the greater omentum must be idiopathic, of no obvious etiologic factor, and spontaneous.

2. The infarction must be primary in the omentum and not accompanied by torsion, trauma, etc., or secondary to some other pathology.

3. The infarction must be segmental, involving only a limited segment of the greater omentum and not involving large areas of the omentum.

4. The infarction must present a typical gross and microscopic picture of the disease.

There have been several different classifications for all cases of acute vascular disturbances of the greater omentum suggested by Leitner et al.,[26] Schaff and Stephenson,[35] and Rose.[34] We suggest the following simple inclusive classification:

A. Primary idiopathic segmental infarction of the greater omentum.
B. Secondary infarction of the greater omentum.
   1. With torsion—
      (*a*) Hernial—external or internal
      (*b*) Nonhernial—associated with postoperative bands or adhesions, trauma, cysts, tumors, infection
   2. Without torsion—
      (*a*) Traumatic—usually direct
      (*b*) Inflammatory — diverticulitis, appendicitis, pelvic infection
      (*c*) Associated with vascular or cardiovascular disease — Buerger's disease, thrombosis of the portal vein, polyarteritis, cardiac disease

Although the etiologic factor and the pathologic findings are rather different in primary and in secondary infarction, the clinical picture of both is undifferentiated in the majority of cases.

Report of Cases

CASE 1.—A 26-year-old white man (truck driver), was admitted to Jersey City Medical Center on Oct. 17, 1957, complaining of acute sudden severe right upper quadrant and epigastric abdominal pain of five days' duration. The pain started while he was driving his truck. On admission the abdominal pain was steady, aching, localized in the right upper quadrant and aggravated by lying flat, breathing deeply, and coughing, and relieved by sitting up. There was no nausea or vomiting, no bowel habit changes, but only slight anorexia. There was no history of previous similar episodes.

Submitted for publication May 9, 1959.

From the Department of Surgery, Jersey City Medical Center.

Professor of Surgery, Seton Hall University School of Medicine, and Chief Surgeon, Medical Center (Dr. Halligan); formerly Senior Resident in Surgery (Dr. Rabiah).

Physical examination revealed definite marked tenderness, rebound tenderness, and rigidity over the right upper quadrant and epigastrium. No palpable masses were present.

Temperature was 36.8 C (98.2 F), pulse 86, respirations 18, and blood pressure 120/80. The white cell count was 7,450 with 61% polymorphonuclears, 35% lymphocytes, 3% monocytes, and 1% eosinophils. Blood chemistry and urinalysis were within normal limits. Serum amylase was 55 units. Electrocardiogram was normal.

Preoperative diagnosis was acute cholecystitis or possible perforated peptic ulcer.

The patient was operated on on the day of admission. The abdomen was opened through a right paramedian incision. A small amount of serosanguineous fluid was found in the right upper abdomen. The gallbladder revealed a slightly thickened wall without signs of acute inflammation or cholelithiasis. There was a well-demarcated bluish area of the greater omentum at its right upper segment measuring 4 by 6 cm., without signs of torsion. The infarcted segment of the omentum was resected, and the gallbladder and appendix were removed.

The pathologic report was infarcted omentum, appendix, and chronic cholecystitis. The microscopic picture of the omentum revealed fatty areolar structure interspaced with loose edematous hyperemic connective tissue, infiltrated with a few polymorphonuclears, lymphocytes, and plasma cells. There were also areas of hemorrhage filled with distorted red blood cells. The small arteries were slightly thick-walled but otherwise normal in appearance. The veins were distended and filled with red blood cells.

The patient made an uneventful recovery and was discharged on the eighth postoperative day.

CASE 2.—A 69-year-old white woman was admitted to the Jersey City Medical Center on Nov. 26, 1957, with the complaint of acute, sudden, moderately severe right lower quadrant abdominal pain, associated with anorexia, nausea, but no vomiting. Hysterectomy had been performed 33 years previously.

Physical examination revealed a slightly distended abdomen with marked tenderness and rebound tenderness over the right lower quadrant. No palpable masses were present, and the peristaltic sounds were slightly hyperactive.

The temperature was 37 C (98.6 F), pulse 98, blood pressure 122/80. The white cell count was 8,000. Blood chemistry and urinalysis were within normal limits. Radiographic studies of the abdomen showed no sign of small bowel obstruction or any other abnormality.

The preoperative diagnosis was acute appendicitis or small bowel obstruction due to adhesions.

The abdomen was explored several hours after admission through a right lower paramedian incision. A moderate amount of serous fluid was found in the peritoneal cavity. A pinkish-red elliptical area, with a well-demarcated border, and measuring 5 by 6 cm., was found in the right lower segment of the greater omentum. No other pathology could be found in the abdomen. There was no sign of torsion in the infarcted segment. The infarcted segment was resected and the abdomen closed.

The microscopic picture of the omentum showed lobulated adipose tissue interspaced by loose edematous congested connective tissue, which supported several distended thin-walled blood vessels, some of which were filled with red blood cells and diffusely infiltrated with polymorphonuclears, lymphocytes, and plasma cells. Areas of extravasated red blood cells were noted. The pathologic diagnosis was infarction of the omentum.

The patient made an uneventful recovery and was discharged on the ninth postoperative day.

CASE 3.—A 71-year-old Negro woman was admitted to the Medical Center on March 22, 1958, complaining of severe left upper quadrant pain of five days' duration with sudden onset. On admission, the pain was localized over an area 8 cm. in diameter in the left upper quadrant, with no radiation or reference, and aggravated by lying flat but relieved by upright position. There was anorexia and nausea but no vomiting. The patient was constipated for several days prior to admission except for a slight bowel movement the previous day. The past history revealed two previous admissions. The first was in Georgia, two years before, for high epigastric pain, and the second to the Jersey City Medical Center, two months previous to the present admission, for mild epigastric pain. On the second admission the patient was worked up completely; two gastrointestinal series, one barium enema, and one gallbladder series were negative. A hysterectomy had been performed in 1939.

Physical examination revealed marked tenderness over a localized area in the left upper quadrant with a very tender, palpable, fairly fixed, and slightly pulsating mass the size of a large grapefruit in the same region. Hypersensitivity of the skin of the abdominal wall over the region was very prominent, and touching that area was painful to the patient. The peristaltic sounds were hypoactive.

The temperature was 39 C (102.2 F), pulse 88, respiration 20, blood pressure 130/80. The white cell count was 7,050; blood chemistry, serum amylase, and urinalysis were within normal limits. Chest x-ray was negative. Electrocardiogram was reported, "in the absence of digitalis S-T changes may be due to myocardial ischemia."

Idiopathic omental infarction was the third provisional diagnosis on admission. It was decided to treat the patient conservatively and to watch

carefully the tender abdominal mass. Treatment consisted of nothing by mouth, intravenous fluids, antibiotics, and bed rest. On the second day the temperature was normal, and the mass was gradually getting smaller and more localized and less tender. Another barium enema and gastrointestinal series with small bowel study were repeated and reported negative. With the aid of all the x-ray studies, the laboratory work, and the clinical course, a final preoperative diagnosis of omental infarction was made by one of us (F. R.)

The abdomen was opened on April 15, 1958, through a left paramedian incision. A very small amount of serous fluid was found in the peritoneal cavity. A localized, moderately firm, necrotic reddish-yellow area was found measuring approximately 8 by 6 cm., irregular in shape, and close to the attachment of the greater omentum to the transverse colon. A thorough abdominal exploration revealed no other pathology. There was no torsion of the omentum in the involved area. The entire necrotic segment was excised, and the abdomen was closed.

The microscopic picture revealed lobulated poorly preserved adipose tissue, interspaced by somewhat edematous loose connective tissue, which supported many polyhedral clear cells with a few lymphocytes, plasma cells, and brownish pigment. The blood vessels were thick-walled and filled with red blood cells. There were areas of extravasations filled with red blood cells. Also noted was proliferation of fibroblasts and foamy macrophages. The pathologic diagnosis was segmental infarction (gangrene) of the omentum, which confirmed our preoperative diagnosis.

The patient made an uneventful recovery and was discharged on the 10th postoperative day.

CASE 4.—A 25-year-old man was admitted to the private service of E. J. H. on Nov. 2, 1958, complaining of right upper quadrant abdominal pain of one day's duration, with nausea but no vomiting. The pain was gradual in onset, becoming severer as time progressed. Previous history revealed left herniorrhaphy and varicocelectomy several years prior.

Physical examination revealed marked tenderness over the right upper quadrant of the abdomen with moderate rigidity. No mass could be palpated.

Temperature was 37.6 C (99.7 F), pulse 84, and blood pressure 130/70. The white cell count was 7,800. The preoperative diagnosis was acute cholecystitis with possible cholelithiasis.

The patient was operated on the day after admission. The abdomen was opened through a right paramedian incision. There was found a small amount of free serous fluid around the right upper quadrant, with a reddish-blue segmental area of the greater omentum measuring approximately 10 by 8 cm. No sign of torsion in the infarcted segment was present. The gallbladder was found to be slightly distended and containing no stones. Cholecystectomy was performed, and the infarcted area of the omentum was excised.

The pathologic report was chronic cholecystitis with acute infarction of the greater omentum. The microscopic picture of the specimen of the omentum showed acute necrosis, edema, interstitial hemorrhages, and severe vascular congestion. The walls of the vessels did not appear diseased and no emboli were detected.

The patient had an uneventful recovery and was discharged on the eighth postoperative day.

Etiology

The precise etiology of idiopathic primary segmental infarction is still unknown. Several theories have been postulated to explain the causative factor in some cases; however, no theory is yet able to account for all cases of this type of infarction. Most authors are in accord with the trauma theory. Totten [41] theorizes that any increased intra-abdominal pressure such as that caused by coughing, sneezing, laughing, especially after ingestion of heavy meals, may be sufficient to cause primary rupture of some of the dependent veins of the omentum, resulting in hemorrhagic extravasation and secondary thrombosis. Pines and Rabinovitch [32] postulated that any stretching or pulling on the omental veins will cause trauma to the endothelial layer, leading to thrombus formation which results in infarction. Harris et al.[17] claimed that this disease is more likely to occur in hypersthenic, obese people, because of their extremely fatty omentum, which by increasing the gravitational pull on the omental veins results in rupture of the vessels. It is thought that the low incidence in children is due to the fact that the omentum is undeveloped and devoid of fat.

Schaff and Stephenson [35] reported a case of a 23-year-old bus driver with omental infarction in which the abdominal pain occurred while he was driving a bus. They suggested that automobile driving may be a factor in initiating the process. The trauma factor is explained by the possibility that

the steering wheel strikes the abdominal wall during sudden stops or jerking movements of the vehicle. We account for the occurrence of omental infarction in our Case 1 for this reason.

Eger and Barto [13] theorize that there is some anatomical peculiarity in the venous drainage of the omentum which could predispose to thrombus formation. It is also possible that its peculiar attachment and free mobility, particularly of its right lower segment, where approximately 75% of the cases of this type of infarction occurs, may be a predisposing factor, the mechanism of which is unknown.

Seley [37] reported, in 1948, a case of a 28-year-old male Puerto Rican who had infarction of the omentum with the presence of polycythemia, which was considered to be a possible contributing factor.

Clinical Features

This disease occurs in all age groups, reported cases ranging from 3 to 71 years; six cases in children under 10, nine cases over 60, with the majority of cases in the third decade of life. The youngest case was reported by Hallstrand [16] and the oldest case by us.

The sex incidence shows predilection for males in a ratio of 2.5:1.

This disease has no characteristic clinical picture to differentiate it from the common causes of acute abdomen. It usually occurs in well-developed, slightly obese individuals. The most prominent and somewhat characteristic symptom is the pain, which is usually severe, sharp, of sudden onset, constant, located in the right lower abdomen, without radiation or reference, aggravated by supine position; and it localizes rapidly and decreases in severity with time. Sometimes it is mild, as a sensation of pressure, or intermittent and colicky. The location of the pain depends on the omental segment involved. It is frequently associated with anorexia and nausea but rarely with vomiting. Bowel habit changes, diarrhea or constipation, have been reported in some cases. It is questionable whether this has any direct relation in these particular cases as a cause or as a result. There is always marked or mild tenderness, and only occasionally rebound tenderness over the region of the infarcted omentum. Hypersensitivity of the skin over the region of tenderness (Ligat's sign), which has been reported in some cases, was found very prominent in our Case 3 and mild in Case 1. There may be, but not necessarily, a palpable mass, which is usually tender at first, poorly localized, superficial, and which gradually becomes demarcated and well localized. Spasticity or rigidity of the abdominal wall over the area involved is a common finding. The temperature is usually within normal limits but may be elevated to 37.8 C-39 C. There is usually some leukocytosis, reported as high as 19,000, but it is not in proportion to the temperature as can be observed from the Table.

A correct preoperative diagnosis is usually not made. There was only suspicion of this diagnosis in one case reported by Alecce et al.[1] (something rare, like an infarction of omentum). In approximately 67% of all reported cases the preoperative diagnosis was acute appendicitis; 19%, acute or subacute cholecystitis; the rest were diagnosed as perforated peptic ulcer, carcinoma of the cecum, carcinoma or diverticulitis of the sigmoid, and pancreatitis or mesenteric thrombosis. We were fortunate to make the correct preoperative diagnosis in Case 3 by way of exclusion and with the aid of previous radiological and laboratory work which had been done on a prior admission.

There have been a limited number of cases collected from the literature. Joss and Pratt [24] in 1948 accounted for 12 cases and added 1. Shea et al.[38] in 1956 collected 43 cases including 6 of their own, which were considered the largest series reported. In reviewing the literature and analyzing all the reported cases, which are summarized and listed in the Table, it still appears that the number of reported cases are few, but we do not believe that the incidence is as

Summary of All Reported Authentic Cases

	Author	Year Reported	Sex	Age	Temperature	White Blood Count	Preoperative Diagnosis
1.	Bush[8]	1896	M	25	37.8 C	N.R.	N.R.
2.	Hunter[20]	1904	F	N.R.	N.R.	N.R.	N.R.
3.	Eberts[12]	1920	M	21	36.8 C	N.R.	Acute appendicitis
4.	Johnson[28]	1932	M	63	37.4 C	15,400	Acute suppurative appendicitis with local peritonitis
5.	Pines & Rabinovitch[44]	1940	M	63	37.4 C	12,400	Acute appendicitis
6.			F	53	37.6 C	10,000	Acute appendicitis
7.			M	40	38.2 C	18,000	Acute appendicitis
8.			M	52	37.4 C.	13,500	Acute appendicitis
9.			M	37	37.6 C.	9,800	Acute appendicitis
10.			F	42	37.8 C.	9,000	Acute appendicitis
11.	Totten[41]	1942	M	27	36.6 C.	N.R.	Acute appendicitis
12.			M	29	38.2 C.	15,000	Acute appendicitis or perforated ulcer
13.	Durando[11]	1945	F	58	N.R.	N.R.	Acute appendicitis
14.	MacKenzie & Small[27]	1945	M	29	37.8 C.	17,600	Acute appendicitis
15.	Cagney & Milroy[9]	1947	M	33	37.4 C.	N.R.	Perforated duodenal ulcer
16.	Harris et al.[17]	1948	M	52	37.0 C.	8,000	Acute appendicitis
17.			M	49	38.0 C.	5,300	Acute appendicitis
18.	Joss & Pratt[24]	1948	F	40	37.0 C.	13,800	Probable atypical acute appendicitis or intrauterine pregnancy
19.	Eger & Barto[16]	1949	F	54	N.R.	Normal	Acute appendicitis
20.	Schaff & Stephenson[31]	1949	M	23	36.8 C.	14,800	Acute appendicitis
21.	Manfredi[26]	1950	F	9	38.2 C.	13,000	Acute appendicitis
22.	Graham & Levinson[15]	1950	M	63	37.8 C.	11,000	Acute appendicitis
23.			M	34	37.8 C.	13,000	Acute appendicitis
24.	Seley[37]	1951	M	28	38.4 C.	10,300	Acute appendicitis
25.	Higgins[18]	1952	M	41	37.0 C.	10,800	Acute appendicitis
26.	Cave[10]	1952	M	47	38.2 C.	13,500	Acute appendicitis
27.	Catanzaro & Farley[9]	1952	M	10	38.0 C.	11,900	Acute appendicitis
28.			F	4	37.8 C.	11,350	Acute appendicitis
29.	Leitner et al.[25]	1952	M	64	Normal	11,900	Possible leaking gastric ulcer, acute pancreatitis, or mesenteric thrombosis
30.	Rachlin[33]	1953	M	54	37.6 C.	12,250	Acute appendicitis
31.			M	23	38.0 C.	13,000	Acute appendicitis
32.	Kerdasha[23]	1953	M	32	37.6 C.	6,500	Acute appendicitis
33.	Tille[43]	1953	M	39	37.4 C.	18,800	Acute appendicitis
34.	Sinow[39]	1953	M	25	37.6 C.	10,800	Acute appendicitis
35.	Hood & Geraci[21]	1953	M	25	37.8 C.	12,300	Acute cholecystitis
36.	Bauman & Hoffert[3]	1954	M	31	38.4 C.	10,900	Acute cholecystitis
37.	Hallstrand[19]	1954	F	54	38.0 C.	11,050	Acute appendicitis
38.			M	11	37.6 C.	11,550	Acute appendicitis
39.			M	52	37.6 C.	10,300	Acute appendicitis
40.			F	3	38.4 C.	11,200	Acute appendicitis
41.	Mitchner[29]	1954	F	5	38.4 C.	17,600	Acute appendicitis
42.	Alecce et al.[1]	1955	M	67	39.0 C.	18,800	Diverticulitis
43.			M	68	37.2 C.	9,950	Subacute cholecystitis
44.			M	22	37.4 C.	8,650	Something rare, as an infarct of the omentum
45.			M	27	37.4 C.	9,700	N.R.
46.			F	60	37.0 C.	8,200	Chronic cholecystitis and cholelithiasis
47.	Rose[34]	1955	F	50	37.8 C.	12,000	Undetermined
48.	O'Beirn[31]	1955	F	32	37.8 C.	N.R.	Acute appendicitis or cholecystitis
49.	Shea et al.[35]	1956	M	51	37.0 C.	6,900	Acute cholecystitis
50.			F	56	37.8 C.	7,550	Acute cholecystitis
51.			M	41	37.6 C.	10,300	Acute cholecystitis with cholelithiasis
52.			F	45	36.3 C.	7,700	Acute cholecystitis with cholelithiasis
53.			M	13	36.6 C.	10,000	Acute appendicitis
54.			F	53	38.0 C.	8,750	Acute appendicitis
55.	Wrizeresinski et al.[45]	1956	M	30	36.8 C.	12,200	Acute appendicitis
56.			M	31	37.6 C.	13,200	Acute appendicitis
57.	Hinshaw & Stafford[20]	1956	M	9	38.0 C.	12,000	Acute appendicitis

Summary of All Reported Authentic Cases—Continued

	Author	Year Reported	Sex	Age	Temperature	White Blood Count	Preoperative Diagnosis
58.	Viar et al.[42]	1957	M	38	N.R.	N.R.	Possible carcinoma of cecum
59.			M	64	N.R.	N.R.	Possible carcinoma or diverticulitis of sigmoid
60.	Bohan[8]	1958	M	32	37.6 C.	16,650	Acute cholecystitis
61.	Halligan & Rabiah	1959	M	26	36.8 C.	7,450	Acute cholecystitis
62.			F	69	36.6 C.	8,000	Acute appendicitis or intestinal obstruction
63.			F	71	39.0 C.	7,050	Infarction of omentum
63.			M	25	37.6 C.	7,800	Acute cholecystitis

N.R.=not recorded.

rare as it seems to be. It is our opinion that the low incidence of reported cases is due to the fact that most cases are not reported, that some of the cases are unrecognized at the time of abdominal exploration, and that some of the cases were treated conservatively and subsided without being subjected to surgery. There are several cases which should not be included in this grouping because either insufficient information was given for evaluation or an etiologic factor was present and obvious: Schottenfeld and Rubinstein,[36] Berger,[4] Nixon,[30] Hines,[19] Cabot Case 28061,[7] Johnson,[23] Eliason and Johnson,[14] and Bauman.[3]

Pathology

The commonest anatomical site of omental infarction is the right lower segment of the greater omentum, which is the richest in fat and most mobile. Other areas of the greater omentum could also be involved, the next commonest being the right upper segment. Both obese and thin omentum could be involved. Grossly, there is usually a slight amount of sanguineous or serosanguineous fluid in the peritoneal cavity, especially around the area of infarction. The infarcted omental segment in most cases is triangular, and its size averages 6 to 8 cm. in diameter. The mass is usually an indurated, well-demarcated, dark yellowish edematous area in the greater omentum, spotted with dark red or blue irregular areas, or occasionally the whole infarcted segment appears red-bluish in color. Sometimes the mass is slightly attached and adherent to the parietal peritoneum by some fibrinous friable, or fibrous, adhesions, depending upon the duration of the lesion prior to surgery. There must be present neither torsion of the entire or any part of the infarcted segment nor other pathology in the abdomen to account for the primary causative lesion with which it is associated.

The microscopic picture is that of omental necrosis with hemorrhagic extravasation into the fatty tissue with thrombosis of all veins and arteries, and infiltration of polymorphonuclears and mononuclear cells, with proliferation of fibroblasts and foamy machrophages in fairly old infarcted omentum. There must be no evidence of any intrinsic vascular or perivascular lesion associated with this pathologic picture.

Treatment

Exploratory laparotomy is usually done in most of the cases because of the difficulty of making a preoperative diagnosis. It is mandatory to explore the greater omentum in every case of acute abdomen in which a suspected lesion is not found. Local resection of the infarcted segment is the treatment of choice. It appears that the infarcted piece of omentum could be left in the abdomen if a correct preoperative diagnosis has been made, but there is always the possibility of some future complication, such as adhesions or abscess formation. Appendectomy has been done in almost all of the reported cases without any effect on the morbidity or mortality.

Prognosis

Prognosis is always good, with rapid and uneventful recovery, especially in this era

of antibiotics. No case of recurrent infarction has been reported. Catanzaro and Farley[9] speculate that the occurrence of omental infarction in childhood could be an evidence of candidacy for future vascular disturbances in the same persons, but as yet there is nothing to substantiate this speculation.

Summary and Conclusion

The subject of primary idiopathic segmental infarction of the greater omentum has been reviewed and all the reported cases have been analyzed, and summarized, making a total of 64 cases, including 4 of our own. An inclusive classification for acute vascular disturbances of the omentum has been suggested. We are reporting the first case to be diagnosed correctly preoperatively. Although this disease has no characteristic clinical picture, a correct preoperative diagnosis can be made by careful observation and evaluation.

76 Tuxedo (3) (Dr. Rabiah).

REFERENCES

1. Alecce, A. A.; Sullivan, S. G., and Ashworth, W.: Spontaneous Idiopathic Segmental Infarction of the Omentum, Ann. Surg. 142:316, 1955.

2. Bang-Dietrichson, O.: A Case of Infarct in Greater Omentum, Nord. med. 12:3413, 1941.

3. Bauman, A., and Hoffert, P. W.: Idiopathic Infarction of the Omentum: Report of 2 Cases, Ann. Int. Med. 42:342, 1954.

4. Berger, A. R.: Hemorrhagic Infarction of the Greater Omentum, Arch. Surg. 36:497, 1938.

5. Bohan, E. B.: Omental Infarction, Delaware M.J. 30:119, 1958.

6. Bush, P.: A Case of Hemorrhage into the Greater Omentum, Lancet 1:286, 1896.

7. Infarction of Portion of Greater Omentum (Cabot Case 28061), New England J. Med. 226: 237, 1942.

8. Cagney, M. S., and Milroy, G.: Idiopathic Infarction of the Omentum, Brit. J. Surg. 35:95, 1947.

9. Catanzaro, F. P., and Farley, J. E., Jr.: Omental Segmental Infarction: A Report of 2 Cases in Children, J. Pediat. 40:240, 1952.

10. Cave, W. H.: Primary Idiopathic Infarction of the Greater Omentum, Illinois M.J. 102: 130, 1952.

11. Durando, A. C.: Primary Infarct of the Greater Omentum, Bol. Soc. cir. Rosario 12:175, 1945.

12. Eberts, E. M.: Case of Spontaneous Hemorrhage from the Greater Omentum, Canad. M.A.J. 10:461, 1920.

13. Eger, S. A., and Barto, R. E., Jr.: Primary Idiopathic Segmental Infarction of the Greater Omentum, Am. J. Surg. 78:518, 1949.

14. Eliason, E. L., and Johnson, J.: Primary Acute Epiploitis, Surgery, 6:68, 1939.

15. Graham, J. A., and Levinson, S. A.: Omental Apoplexy: Idiopathic Segmented Infarction of the Greater Omentum, Am. J. Digest. Dis. 17:114, 1950.

16. Hallstrand, D. E.: Primary Omental Infarction, Am. J. Surg. 87:563, 1954.

17. Harris, F. I.; Diller, T., and Marcus, S. A.: Hemorrhagic Infarction of the Greater Omentum Simulating Acute Appendicitis: A Report of 2 Cases, Surgery 23:206, 1948.

18. Higgins, G. A.: Idiopathic Spontaneous Segmental Infarction of the Omentum, A.M.A. Arch. Surg. 64:395, 1952.

19. Hines, L. E.: Hemorrhagic Infarction of the Greater Omentum, Illinois M.J. 66:166, 1943.

20. Hinshaw, D. B., and Stafford, C. E.: Idiopathic Segmental Infarction in a Child, California Med. 85:339, 1956.

21. Hood, R. T., Jr., and Geraci, J. E.: Infarction of Omentum Simulating Acute Cholecystitis: Report of Case, Proc. Staff Meet. Mayo Clinic 28:296, 1953.

22. Hunter, C. H.: Hematoma or Apoplexy of the Omentum, Northwest. Lancet 24:228, 1904.

23. Johnson, A. H.: The Greater Omentum and Omental Thrombosis, Northwest Med. 31:285, 1932.

24. Joss, C. S., and Pratt, J. H.: Primary Idiopathic Segmental Infarction of the Greater Omentum, Minnesota Med. 31:996, 1948.

25. Kerdasha, R.: Idiopathic Spontaneous Segmental Infarction of the Greater Omentum, Ann. Surg. 137:419, 1953.

26. Leitner, M. J.; Jordan, C. G.; Spinner, M. H., and Reese, E. C.: Torsion, Infarction and Hemorrhage of the Omentum as a Cause of Abdominal Distress, Ann. Surg. 135:103, 1952.

27. MacKenzie, W. C., and Small, J.: Primary Idiopathic Segmental Infarction of the Greater Omentum, Canad. M.A.J. 55:144, 1946.

28. Manfredi, D. H.: Omental Segmental Infarction in Infancy: Report of Case, Arch. Pediat. 67:247, 1950.

29. Mitchner, J. S.: Omental Infarction, Surgery 36:1148, 1954.

30. Nixon, W. C. W.: Hematoma of the Gastro-Colic Omentum, Brit. M.J. 1:797, 1932.

31. O'Beirn, S. F.: Primary Infarction of the Greater Omentum, J. Irish M.A. 36:24, 1955.

32. Pines, B., and Rabinovitch, J.: Idiopathic Segmental Infarction of Greater Omentum, Surg. Gynec. & Obst. 71:80, 1940.

33. Rachlin, S. A.: Primary Idiopathic Segmental Infarction of Greater Omentum, J. Internat. Coll. Surgeons 19:359, 1953.

34. Rose, T. F.: Primary Acute Inflammation and Primary Idiopathic Infarction of the Greater Omentum, M.J. Australia 2:278, 1955.

35. Schaff, B., and Stephenson, H. U., Jr.: Omental Infarction Simulating Acute Appendicitis, North Carolina M.J. 10:361, 1949.

36. Schottenfeld, L. E., and Rubinstein, H.: Hemorrhage and Thrombosis of the Omentum: Their Etiology in the Acute Abdomen, Am. J. Surg. 51:449, 1941.

37. Seley, G. P.: Primary Idiopathic Segmental Hemorrhagic Infarction of the Greater Omentum, J. Mt. Sinai Hosp. 17:523, 1951.

38. Shea, C. J.; Power, F. A., and Spellman, J. W.: Idiopathic Segmental Infarction of the Greater Omentum: Report of 6 Cases and Review of the Literature, New England J. Med. 254:263, 1956.

39. Sinow, G. S.: Idiopathic Segmental Infarction of the Greater Omentum, Am. J. Digest. Dis. 20:43, 1953.

40. Tille, R. J., Jr.: Idiopathic Segmental Hemorrhagic Infarction of the Greater Omentum, Ann. Surg. 138:279, 1953.

41. Totten, H. P.: Primary Idiopathic Segmental Infarction of the Greater Omentum, Am. J. Surg. 56:676, 1942.

42. Viar, W. N.; Donald, J. M., and Berery, K.: Idiopathic Omental Infarction, Ann. Surg. 146:876, 1957.

43. Wrizeresinski, J. T.; Firestone, S. D., and Walske, B. R.: Primary Idiopathic Segmental Infarction, Surgery 39:663, 1956.

Choledochocolic Fistula

A Case Report

LAWRENCE G. HAMPSON, M.D., F.R.C.S. (C), and GEOFFREY LEHMAN, M.D., Montreal, Canada

Internal biliary fistulas may arise from peptic ulceration, operative trauma or, most commonly, as a result of biliary disease with associated calculi. Of the latter group the most frequently seen is the communication between the gallbladder and the upper small bowel through ulceration of a gallstone into the duodenum; this may result in gallstone ileus. Less commonly fistulas develop between the common bile duct and the duodenum from stones in the duct eroding into the bowel or from the penetration of a peptic ulcer into the common duct.

Uncommon too are the fistulas between the biliary tract and the colon. In 1925 Judd and Burden [4] reported 26 cholecystocolic fistulas as part of a series of 153 cases of internal biliary fistula seen at the Mayo Clinic. In one of the 26 the diagnosis had been made preoperatively by barium enema. Bernhard [1] reported 36 of 109 internal biliary fistulas to involve the colon. After 1935 several reports were published of the preoperative diagnosis of cholecystocolic fistula by barium enema,[3,5,7-9] but in 1949 Marshak [5] was able to find only 12 cases in which the diagnosis had been made preoperatively in this way.

We have been able to find reports of only two cases of choledochocolic fistula in the literature. In 1935 Meese [6] published a case of postoperative choledochocolonic fistula following a cholecystectomy which had been complicated by a fecal fistula. The diagnosis was made radiologically by barium enema prior to operative correction of the fistula. In 1946 a case reported from the Massachusetts General Hospital [2] listed under the autopsy findings a choledochoduodenocolic fistula. The protocol described two fistulas, one from the common bile duct to the duodenum and one from the common duct to the colon. The diagnosis had not been made either preoperatively or at the time of surgery.

Submitted for publication May 7, 1959.

From the Department of Surgery, Montreal General Hospital and McGill University.

Report of Case

A 52-year-old white man was admitted to the Montreal General Hospital on Feb. 17, 1955, complaining of vomiting and epigastric pain which had begun in the morning of the day of admission. The pain radiated to the left shoulder. There was no history of similar symptoms before the onset of this episode.

On examination he appeared well developed and nourished. The skin was jaundiced. The tongue was coated and moist. Tenderness was present in the epigastrium. The stool was yellow. The urine was dark and strongly positive for bile. The hemoglobin was 13 gm. % and the white cell count 16,000 per cubic millimeter.

The serum bilirubin on the day of admission was 4.0 mg. %; cephalin cholesterol flocculation negative; alkaline phosphatase 5 units, and the diastase less than 3 units. An oral cholecystogram revealed no concentration of dye by the gallbladder, but one radio-opaque calculus was seen.

A diagnosis of acute cholecystitis was made, and the patient was fasted and kept in bed. Analgesics, antispasmodics, and intravenous fluids were given as required. As he improved he was permitted a low-fat diet. On March 2 an intravenous choledochogram was attempted, but the ducts were not visualized. On March 4 cholecystectomy and choledochostomy were done. One stone was found in the gallbladder. Ten were recovered from the common bile duct. An operative choledochogram was done after exploration of the duct with instruments. The films showed no residual stones. A short-arm T-tube was placed in the duct and the wound was closed. The patient did well postoperatively and his jaundice disappeared.

A T-tube choledochogram done on March 21, the 17th postoperative day, revealed dilatation of the common duct and several areas of translucency. The right hepatic duct was not visualized. These films were interpreted as indicating the presence of residual stones in the common duct. The patient was discharged home on March 24, elective readmission being arranged for the removal of his retained stones.

He returned to hospital on April 14. He reported being perfectly well in the interval with good drainage from the T-tube. Physical examination was negative. The urine and stool were normal. The hemoglobin was 13.1 gm. %; serum bilirubin 0.1 mg. %; total protein 7.2 gm. %; albumin 3.1, and globulin 4.1 gm. %.

A T-tube choledochogram was done on April 18. The common duct was patent and contained a stone. The right hepatic duct again failed to fill.

On April 20 a choledochostomy and duodenotomy were done. Three stones were recovered from the ducts, two from the upper part of the common duct and one from the ampulla. Dilators could not be passed into the duodenum and radiopaque dye injected into the duct was not seen in the bowel. The duodenum was therefore opened and the sphincter of Oddi was dilated from below to 5 mm. A short-arm T-tube was placed in the duct and the wounds were closed.

The patient made an uneventful recovery. A T-tube choledochogram done on May 10, however, revealed an oval filling defect in the common duct and, as before, the right hepatic duct did not fill.

He was discharged on May 12 with instructions as to irrigation of his T-tube and was booked for readmission for a further procedure for retained common duct stone.

After discharge he continued to feel perfectly well and did not return to hospital for over three years. During this time he gained 40 lb. in weight. He continued to irrigate the T-tube with saline daily before retiring. Early in August, 1958, he began to have frequent bowel movements, passing five or six semisolid stools daily. They were light brown and contained no blood. He experienced no pain and his appetite was good. In September, 1958, he developed a dry cough. On Sept. 21 he began to raise white frothy sputum and on the day of admission, Sept. 24, the cough increased. During one episode of forceful coughing the T-tube was expelled through the abdominal wall. At this time he became short of breath, and felt pain in the epigastrium and behind the lower sternum.

On examination he was of good color, coughing and sitting up in bed, breathing rapidly. The sputum was rusty brown and frothy. There was dullness at both lung bases with rales and diminished breath sounds. The pulse was 84 and regular. The blood pressure was 100/75. The abdomen was obese. Through a long right paramedian scar a large incisional hernia protruded. A fistula opened lateral to this where the T-tube had been, from which clear bile drained. The liver was not palpable. On rectal examination yellowish fluid was seen on the gloved finger.

The hemoglobin was 14 gm. %; the white cell count 9,600 per cubic millimeter. The serum bilirubin was 0.4 mg. %; total protein 6.4 gm. %, albumin 3.9, and globulin 2.5 gm. %; alkaline phosphatase 3 units, and cephalin cholesterol flocculation 1+. Sulfobromophthalein (Bromsulphalein) retention was 25% in one hour.

Chest x-rays showed cardiac enlargement, small bilateral pleural effusions, and pulmonary edema.

Barium enema showing filling of biliary tree through choledochocolic fistula.

Plain films of the abdomen revealed questionable gas in the biliary tract.

A diagnosis of bronchopneumonia with congestive heart failure was made and he was treated for this on the medical service for three weeks. During this time the external biliary drainage ceased. A barium enema showed barium flowing up the common bile duct from the hepatic flexure and completely outlining the biliary tree (Fig. 1). It is noteworthy that the right hepatic duct, which had failed to fill at all previous examinations, was clearly seen in these films. The fistula joined the transverse colon a short distance distal to the hepatic flexure.

On intravenous choledochogram the bile ducts were not visualized. Barium meal was normal except for the presence of a diverticulum of the third portion of the duodenum.

On Oct. 27 the patient was operated on for the correction of his choledochocolic fistula and incisional hernia. The fistula was found between the anterior aspect of the midportion of the common duct and the posterior aspect of the transverse colon a short distance from the hepatic flexure. At the level of the fistula the common duct was angulated somewhat to the left, but entered the duodenum normally. It was somewhat dilated. One oval stone, 1.0 by 0.5 cm. was present at the ampulla of Vater. The fistula was broken down and the opening in the colon closed. A short longitudinal incision was made in the common duct above the entrance of the fistula, and through both openings the duct was probed and the stone removed. The sphincter of Oddi was dilated to 8 mm. without difficulty. A T-tube was placed in the common duct and both openings in the duct were closed with interrupted sutures of 00 chromic catgut. It was then found necessary to remove some 4 in. of the proximal transverse colon as its blood supply had been compromised during the dissection of the fistula. Resection and end-to-end anastomosis were carried out without event.

The T-tube and a large cigarette drain were brought out the upper end of the wound and the ventral hernia was repaired in closing. The patient made a satisfactory recovery. He began eating on the third postoperative day and the bowels moved normally. Clear bile drained from the T-tube, which was removed at the end of the fourth week, after a normal T-tube choledochogram. He was last seen on Jan. 11, 1959, when he felt perfectly well.

Comment

When the patient was questioned as to why he had not returned for his third operation in 1955, or to enquire about the likelihood of removal of his T-tube, he said simply that he had felt well and so had not bothered. Presumably the onset of his frequent stools six weeks prior to the last admission marked the opening of the fistula. There were no signs or symptoms to suggest cholangitis.

Gas was visible in the biliary tract on plain films of the abdomen, suggesting a fistula to the bowel. Barium enema confirmed this with a striking outline of the whole biliary tree (Fig. 1).

One other noteworthy point is the length of time the patient kept his latex T-tube in place. He had irrigated it carefully every day with saline. It never became blocked and showed no degeneration or crusting when he presented it on admission. The onset of the bronchopneumonia and the forceful expulsion of the T-tube by a cough were presumably fortuitous.

Cholecystoenteric fistulas arise as a rule through the erosion of a stone through the gallbladder wall. The precise etiology of the fistula here presented remains open to question. It would seem that the fistula developed at the time of onset of diarrhea six weeks prior to his last admission. If this were the case, it would be difficult to ascribe it to previous operative trauma. Spontaneous internal fistulas may develop between the common duct and the bowel following a period of obstructive jaundice, but no history of jaundice was elicited. It should be noted that two calculi had previously been reported in the duct, one of which was obstructing the right hepatic duct. Only one stone was removed at operation, the right hepatic duct being demonstrably patent subsequently. It is suggested that one of the two calculi had eroded through the duct to give rise to the fistula.

The possibility of implication of the T-tube in fistula formation must be considered, but although it had remained in situ for three years the lack of crusting and its apparent malleability would be against this.

All authors seem to be in agreement that the diagnosis of cholecytocolic fistula is

most frequently made by barium enema but the preoperative diagnosis is seldom made. It would appear that choledochocolic fistula also requires barium enema for its demonstration, as was shown by Meese [6] and by us. The presence of gas in the biliary tree should suggest the use of a barium enema in making a specific diagnosis. Danzer [3] was able to find only one report of complete filling of the bile ducts at barium enema prior to 1937, though this had doubtless become commoner since. The absence of signs and symptoms of cholangitis in the presence of biliary colic fistulae would seem to be the rule rather than the exception, and it has been questioned whether operative correction is desirable. The case reported by Meese [6] showed no evidences of cholangitis during the year and a half that the fistula was present, but diarrhea was continuous during that period. Our case showed similar symptomatology though of shorter duration. Possibly complete diversion of bile into the colon may consistently give rise to diarrhea, making operative correction of the fistula most desirable.

Summary

A case of choledochocolic fistula is presented. It is thought to have formed three years after a second operation for choledocholithiasis. It is felt that the fistula was caused by erosion of a calculus through the common bile duct into the adjacent colon.

The diagnosis was made by barium enema prior to operative correction.

We were able to find only two other reports of this condition in the literature.

REFERENCES

1. Bernhard, F.: Die spontanen inneren Gallenfisteln und ihre operative Behandlung, Deutsche Ztschr. Chir. 242:493, 1934.

2. Benign Stricture of Common Bile Duct: Choledochoduodenocolic Fistula, Mass. Gen. Hosp. Case 32311, New England J. Med. 235:168, 1946.

3. Danzer, J. T.: The Preoperative Diagnosis of Cholecystocolonic Fistula, Radiology 28:88, 1937.

4. Judd, E. S., and Burden, V. G.: Internal Biliary Fistula, Ann. Surg. 81:305, 1925.

5. Marshak, R. H., and Henkin, W.: Cholecystocolic Fistula, Radiology, 53:555, 1949.

6. Meese, J.: Postoperative Choledochus-Kolonfistel, Röntgenpraxis 7:690, 1935.

7. Medelman, J. P.: Cholecystocolic Fistula, Am. J. Roentgenol. 36:52, 1936.

8. Podlasky, H. B.: Biliary Colic Fistula, Radiology 24:345, 1935.

9. Stevensen, C. A., and Sherwood, M. W.: The Roentgen Diagnosis of Cholecystocolic Fistula, Radiology 35:616, 1940.

Femoral Hernia in Infancy and Childhood

ASCHER LAWRENCE MESTEL, M.D., M.S. (Surg.); MORTON G. FARBER, M.D., and IRWIN CHABON, M.D., Brooklyn

Femoral hernia in the infant or child is a condition which is found infrequently. Only 0.4% [1,2] to 0.6% [3] of all hernias in children will be of the femoral variety. In a total of 3,395 adult hernioplasties performed in several general hospitals, 3.3% were femoral.[4] It is therefore evident that there is a significant increase in the incidence in the adult as compared with the child. Many [5] believe that femoral hernias are never congenital. Because of this belief and because we felt there was no recent review of the subject, we undertook a study of femoral hernias in children. We have observed two femoral hernias in children in the last five years.

Report of Cases

CASE 1.—A 9-year-old white boy was admitted on Dec. 3, 1953, because of a right inguinofemoral mass of two months' duration. There had been no associated pain, nausea, or vomiting. At times, it was difficult to reduce the mass. Past history was noncontributory.

Physical examination revealed a nonpulsatile, nonreducible, slightly tender mass below the right inguinal ligament and over the femoral ring. There was no impulse palpated upon straining.

The diagnosis of right femoral hernia was made, and the child was operated on Dec. 4, 1953. An oblique incision over the femoral mass with a 2.5 cm. extension along the inguinal ligament was made. A hernial sac, 3 cm. in greatest length, was found protruding from the femoral canal. The neck was 1.0 cm. in width. The sac was opened and no contents noted. It was ligated at its base and excised. The hernia was repaired by approximating the inguinal ligament to Gimbernat's ligament and to the pectineus fascia. The patient had an uneventful postoperative course, leaving the hospital on the fifth postoperative day. There is no recurrence five years postoperatively.

Submitted for publication May 25, 1959.

From the Department of Surgery Beth-El Hospital.

CASE 2.—A 3-year-old white boy admitted on Nov. 14, 1958, because of a left inguinal mass of two months' duration. The mass was asymptomatic. Past history was noncontributory.

Physical examination revealed a small firm mass palpable in the left femoral region and a dilated left external inguinal ring.

The diagnosis of left inguinal hernia with femoral node or femoral hernia was made. Operation was performed on Nov. 16, 1958. An incision above and parallel to Poupart's ligament was made and a very small indirect hernia was noted. This was dissected free, ligated, and excised. The femoral area was then explored through the same incision and a hernial sac, 5.0 cm. in length, was found. Transversalis fascia was opened and the femoral hernia converted into a direct inguinal hernia. The sac contained omentum. A high ligation of the sac and a Cooper ligament repair were performed. The postoperative course was uneventful. There was no recurrence as of February, 1959.

Comment

Incidence.—As can be seen from Table 1, a cumulative study of 6,416 hernias in children, only 29 were femoral. This is an incidence of 4.5 per 1,000.

Side Involved.—Unfortunately we do not have information as to the side involved in all cases. Three patients had bilateral; five had right, and two left femoral hernias. From the small number of cases, we cannot draw any conclusions as to frequency of side involved.

TABLE 1.—*Incidence of Femoral Hernia*

Author	No. of Herniotomies in Children	No. of Femoral Hernias
Herzfeld [1]	1,000	4
MacLennan [2]	1,000	6
Owen [4]	220	1
Ribera y Sans [7]	3,098	14
Rutherford [3]	1,098	4
Total	6,416	29

TABLE 2.—*Age of Appearance of Hernia*

Age, Yr.	No. of Cases
1-5	19
6-15	129

Age.—The only large series studied in which the age was first noted was made by Murray [8] and Denoeux.[9]

As can be seen from Table 2, there is a sharp increase after the age of 5. The youngest child reported is a 5-week-old boy with a strangulated femoral hernia.[10]

Sex.—A study of the literature in which single case reports alone have been recorded discloses six males and only one female.[3,10-15] Adding our own two cases, there would be eight males and one female. However, if the larger series are considered [1,2,16] and added to the individual case reports, there are 56 females and 21 males in which the sex is mentioned.

Etiology.—The earlier in life that a hernia appears, the greater the possibility that it is congenital. There have been at least 19 cases reported of femoral hernia in children below the age of 5. It is difficult to consider these hernias acquired. These children bore no children, were not manual laborers, nor did they have chronic cough, the common etiological factors implicated in the acquired femoral hernia. For femoral hernias to be considered congenital, we must be able to prove that a preformed sac is present. In a study of 200 consecutive autopsies with no evidence of hernia, in 47 of the bodies 52 femoral diverticula were present.[8] In 14 instances they were bilateral. Unfortunately, the number of femoral diverticula found in autopsies of newborn infants is not discussed. One of the cases was in a child of 7 years with bilateral femoral diverticula. It is only in the new-born infant or in the young child that we can be certain that the sac is congenital and not acquired.

TABLE 3.—*Sex Incidence of Femoral Hernia in Children*

Author	Male	Female
Coley [16]	11	48
Herzfeld [1]	1	3
Rutherford [2]	1	4
Pooled individual cases	8	1
Total	21	56

Tasche believes that femoral sacs are never congenital but are always acquired.[5] He autopsied 64 premature and newborn infants, as well as 8 young children, and found no femoral sacs. The number of cases studied is certainly much too small to draw any conclusions. Since the incidence of femoral hernia is only 4.5 per 1,000 of all hernias in children, a much larger group of cases must be investigated. We think we can safely say that femoral hernias can be congenital, as evidenced by their appearance in young children. In the adult, the congenital or acquired variety may be present. We know no way of differentiating the congenital or acquired type in the adult. There is no analogous indirect (congenital) or direct (acquired) form as with inguinal hernias.

Differential Diagnosis.—Inguinal hernia and or hydrocele are most commonly considered. Other possibilities are lymphadenopathy, varix of the saphenous vein, lipoma, cystic hygroma, psoas abscess, ectopic testis, and obturator hernia. In order to make the diagnosis, one must be aware of the fact that femoral hernias do occur in infants and children. More often than not, the femoral hernia is called an inguinal hernia, and only at operation is the true pathology noted.

Strangulated Femoral Hernia.—Up to 1954, there have been five reports [10] of strangulated femoral hernias below the age of 10 years.

Contents of Sac.—Almost all of the abdominal viscera, with the exception of the spleen and liver, have been found in the adult femoral hernia sacs.[17] The femoral hernial sac in the child may be empty. Omentum,[2,15] ovary and tube,[9,14] small in-

testine,[10,14] and cecum [11] have been reported in the femoral sac of children.

Treatment.—No one has had sufficient experience or has studied enough cases to say that only a high ligation of the sac will cure a congenital femoral hernia in a child. There haven't been any good studies or follow-ups reported. Of the 14 cases that Coley [16] followed, 2 patients developed recurrences, an incidence of 14.2%. He simply ligated the hernial sac. Many authors have also been satisfied with a high ligation.[1,10,13] MacLennan,[3] in addition to the ligation of the sac, utilized a bone staple in approximating the inguinal ligament to the pubis. In 1920, Cumston [18] suggested a high ligation of the sac, plus suturing the conjoined tendon to Cooper's ligament.

It seems logical to us to approach these hernias through an inguinal crease incision, opening the external oblique aponeurosis, and exploring the inguinal canal for an inguinal hernia. The transversalis fascia is then incised and the femoral hernial sac converted into a direct inguinal hernia. The sac contents are reduced if present, and a high ligation of the sac performed. The transversalis fascial defect is repaired by approximating the transversalis fascia to Cooper's ligament out to the femoral vein. The external oblique aponeurosis is reconstructed with 000 chromic atraumatic suture. Subcutaneous tissue is closed with 0000 interrupted plain absorbable surgical suture (catgut), and skin with 0000 continuous subcuticular plain absorbable surgical suture. A collodion dressing is applied.

Summary and Conclusions

Two cases of femoral hernia in children are reported.

The incidence of femoral hernia in children is 4.5 per 1,000 hernias.

No definitive conclusions can be drawn as to which side is involved most frequently.

The hernia is much more frequent in the 6-15-age group than the 1-5-year group.

More cases have been reported in the female than in the male.

Femoral hernias can be congenital, as evidenced by their appearance in infants.

The treatment of choice is a high ligation of the sac and repair of the transversalis fascia by approximating it to Cooper's ligament.

50 Plaza St. (38).

REFERENCES

1. Herzfeld, G.: Hernia in Infancy, Am. J. Surg. 39:422-428, 1938.

2. Rutherford, R.: Femoral Hernia in Children, Lancet 2:498, 1927.

3. MacLennan, A.: The Radical Cure of Femoral Hernia in Children, Glasgow M. J. 96: 83-87, 1921.

4. Davis, L., Editor: Christopher's Textbook of Surgery, Ed. 6, Philadelphia, W. B. Saunders Company, 1956, p. 506.

5. Tasche, L. W.: Etiology of Femoral Hernia, Arch. Surg. 25:749-782, 1932.

6. Owen, H. W.; Kirklin, J. W., and Du Shane, J. W.: Femoral Hernias in Infants and Young Children, Surgery 36:283-285, 1954.

7. Ribera y Sans, J.: Hernie de l'Enfant, presented at the 11th Congress of the Société-Internationale de Chirurgie; cited by Rutherford.[2]

8. Murray, R. W.: Is the Sac of a Femoral Hernia of Congenital Origin or Acquired? Ann. Surg. 52:668-677, 1910.

9. Denoeux, L.: Crural Hernia in Children, Thesis, Bordeaux, 1908; cited by Shepler, and Smith.[14]

10. Underhill, B. M. L.: Strangulated Femoral Hernia in an Infant Boy Aged 5 Weeks, Brit. J. Surg. 42:332-333, 1954.

11. Coley, W. B.: Double Femoral Hernia in Male Child Aged 2 Years, Ann. Surg. 26:246, 1897.

12. Fitzwilliams, D. C. L.: Case of a Boy Aged 5 Years with 2 Femoral Herniae, Proc. Roy. Soc. Med. 7:20, 1914.

13. Lloyd, E. I.: Femoral Hernia in a Boy of 5 Years, Brit. J. Surg. 18:657, 1931.

14. Shepler, N. B., and Smith, C. W.: Femoral Hernia in Infancy, Am. J. Surg. 49:375-377, 1940.

15. Temple, J. L.: Strangulated Femoral Hernia in a Young Boy, Lancet 1:594, 1952.

16. Coley, B. L.: Three Thousand Consecutive Herniotomies, Ann. Surg. 80:242-255, 1924.

17. Balch, F. G.: Femoral Hernia, New England J. Med. 216:385-388, 1937.

18. Cumston, C. G.: The Radical Cure of Femoral Hernia in Children, Clin. J. 49:425-426, 1920.

Primary Neoplasms of the Small Bowel*

Analysis of One Hundred Two Cases

A. C. BRODERS Jr., M.D.; N. C. HIGHTOWER Jr., M.D.; W. H. HUNT III, M.D.;
J. C. STINSON, M.D.; R. R. WHITE, M.D., and HENRY LAURENS Jr., M.D., Temple, Texas

Introduction

During the professional lifetime of most physicians, tumors of the small bowel are rarely encountered. Though the small bowel accounts for roughly 75% of the length of the alimentary canal, yet only 3% to 6% of gastrointestinal neoplasms occur in this portion of it. Furthermore, the importance of these tumors and their early detection is underscored by the fact that 75% of them are malignant. Many of these tumors produce early symptoms, and, if they are recognized, surgical resection can result in a reasonably good expectation of a cure.

An early clinical diagnosis of these tumors is possible if the physician is "small bowel conscious" when frank or occult blood is found in the stools, in the presence possibly of an unexplained anemia. It should also be remembered that the location, size, and behavior of the tumor determines the nature of the symptomatic onset and the ultimate clinical course. The symptom complex elicited from the patient may be vague and poorly delineated, as well as considerably variable from patient to patient afflicted with this neoplasm. The symptoms, furthermore, whether the tumor be benign or malignant, are often not discernibly different. A palpable mass is frequently not felt. Though the onset of the disease is usually subtle and insidious, yet hemorrhage or perforation may be the first sign of trouble. Intestinal obstruction of varying grades and types may be encountered. Intussusception is a common form of obstruction among these growths. Usually, however, the patient's complaints are less dramatic and include abdominal distention or bloating, postprandial fullness, malaise, loss of sense of well-being, nausea, borborygmus, anorexia, weight loss, and vague colicky or cramping pains. The pains tend to be more localized to the periumbilical region. More often than not, these complaints are attributed by the attending physician to functional indigestion. Negative roentgenograms of the small bowel do not exclude tumor since the small intestine is of relatively great length and difficult to fill homogeneously with barium.

Unfortunately, by the time a typical clinical picture appears, permitting a preoperative diagnosis of a small bowel tumor, the lesion is often too far advanced to permit a surgical cure. Hence there is still a paucity of those patients fortunate enough to survive beyond the five-year limit. Though far from infallible, certain signs and symptoms help one to localize the neoplasm, once its presence in the small bowel is suspected. A tumor of the first portion of the duodenum may simulate an ulcer in behavior, even with radiation of pain through to the back. Failure of response to ulcer therapy should increase one's suspicion of a duodenal growth. Jaundice of an obstructive nature with concomitant pruritus, pain, and weight loss should focus attention on an ampullary lesion. Lower in the intestinal tract, obstructive symptoms are commoner, with attacks of colicky pain coming at increasingly frequent intervals.

Received for publication June 15, 1959.

* Surgery Illustrated. Shown as a scientific exhibit at the 107th Annual Meeting of the American Medical Association, San Francisco, June 23-27, 1958.

It should be emphasized that the physician should be more small bowel conscious, and surgical exploration should be performed early if at all possible.

The present study was undertaken to review the experience with small bowel tumors at the Scott and White Clinic. The study, exclusive of the primary adenocarcinomata of the ampulla of Vater, covers a 15-year period prior to July, 1956. The ampullary tumors represent this clinic's experience from 1924 to 1956. The total number of tumors presented is 102.

Conclusions

1. Approximately 50% of benign neoplasms of the small bowel do not produce symptoms.

2. The commonest symptoms of neoplasms of the small bowel are pain, weight loss, vomiting, weakness, bleeding, and alteration of bowel habits. Pain is usually cramping and midabdominal, may be dull and diffuse.

3. The appearance of jaundice tends to localize the neoplasm to the duodenum or to the ampulla of Vater.

4. Symptoms may be obscure, and early diagnosis is often difficult.

5. The commest physical findings of neoplasm of the small bowel are abdominal tenderness, abdominal distention, and a palpable mass.

6. The examination of the stool for occult blood is the most important single laboratory test.

7. Roentgenologic examination is positive in approximately 50% of all neoplasms of the small bowel. Roentgenologic examination of the small bowel should be used more frequently.

8. The accuracy of roentgenologic examination decreases from the duodenum to the ileum.

9. Survival is related to the location, type, and grade of neoplasm, and to the presence or absence of metastasis.

10. Adenocarcinoma of the small bowel has a better prognosis than lymphosarcoma of the small bowel.

11. The prognosis is better if the neoplasm is located in the jejunum or ileum than in the duodenum.

12. Lymphosarcoma occurs more commonly in the lower than in the upper small bowel.

13. Roentgen therapy apparently does not prolong survival.

14. We must be more aware of primary neoplasm of the small bowel. Early surgical exploration is necessary when a neoplasm of the small bowel is suspected, if we are to improve the survival rate.

Scott and White Clinic.

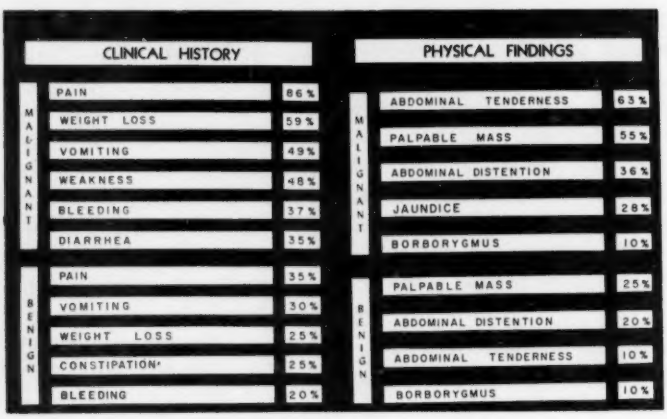


Figure 1

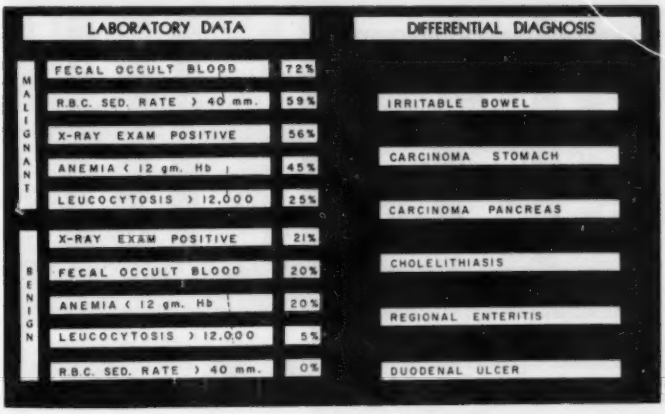


Figure 1 (cont'd)

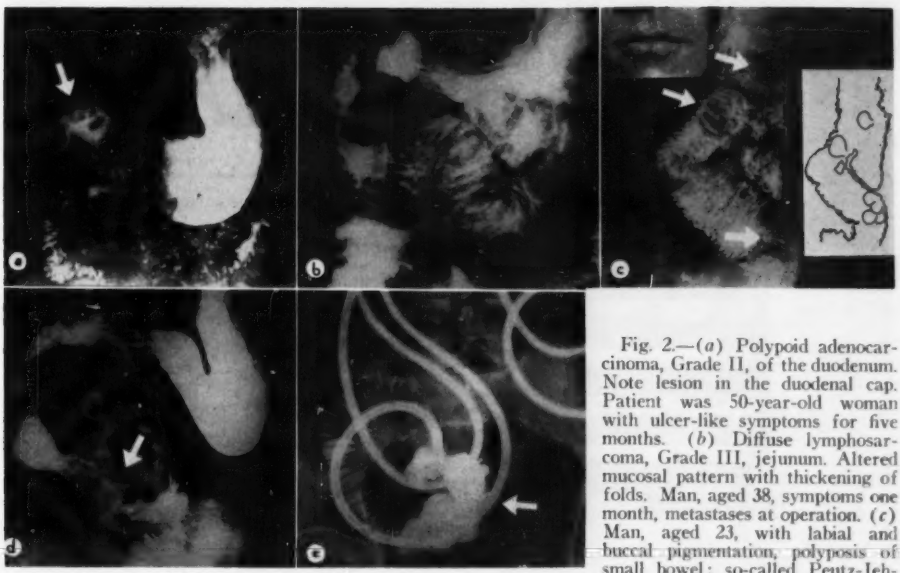


Fig. 2.—(*a*) Polypoid adenocarcinoma, Grade II, of the duodenum. Note lesion in the duodenal cap. Patient was 50-year-old woman with ulcer-like symptoms for five months. (*b*) Diffuse lymphosarcoma, Grade III, jejunum. Altered mucosal pattern with thickening of folds. Man, aged 38, symptoms one month, metastases at operation. (*c*) Man, aged 23, with labial and buccal pigmentation, polyposis of small bowel; so-called Peutz-Jehgers' syndrome. (*d*) Annular constricting adenocarcinoma, Grade II, of jejunum. Man aged 42, had symptoms for 12 months. Metastases at operation. Patient lived 18 months (*e*) Obstructing lymphosarcoma, Grade II, of terminal ileum. Lesion demonstrated after intubation and injection of medium through tube.

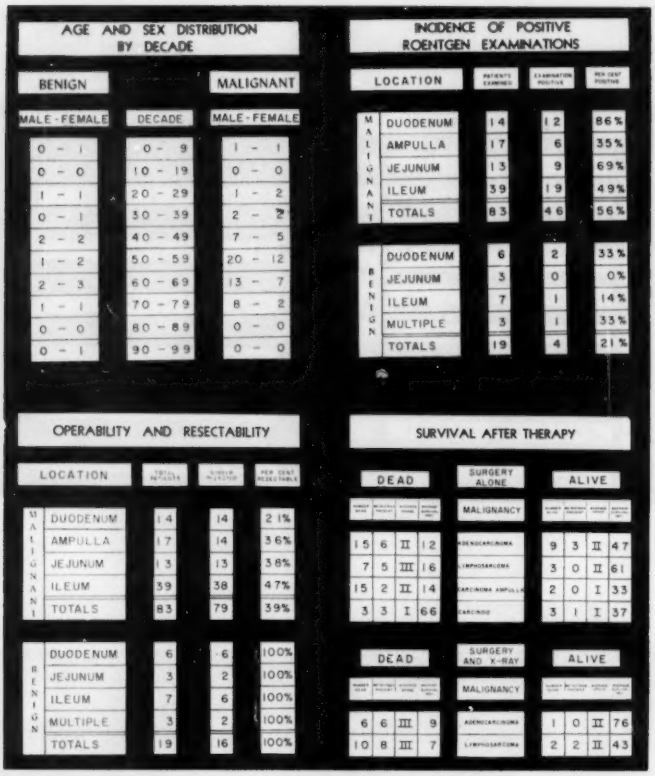


Figure 3

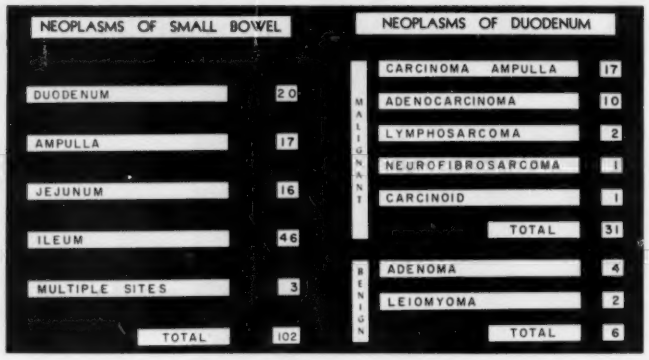


Figure 4

Fig. 5.—(*a*) Ileum—adenocarcinoma; reduced about 40% from mag. × 195. Carcinoma is still in situ in this section, and histologic characteristics of carcinoma are apparent in contrast to normal mucosa. (*b*) Ileum—lymphosarcoma; reduced about 40% from mag. × 123. A characteristic of this type of tumor in the intestine is that it infiltrates muscle and mucosa, but ulceration of mucosa is a relatively late occurrence. (*c*) Ampulla of Vater—papillary adenocarcinoma; reduced about 40% from mag. × 300. Usually of low-grade of malignancy, but prognosis poor because of location. (*d*) Ileum—hemangioma; reduced about 40% from mag. × 105. Tumors of this type may be single or multiple, are important as a source of hemorrhage, and must be considered in differential diagnosis.

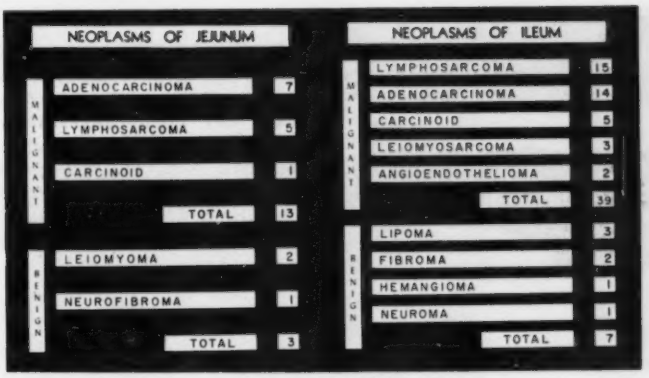


Figure 4 (cont'd)

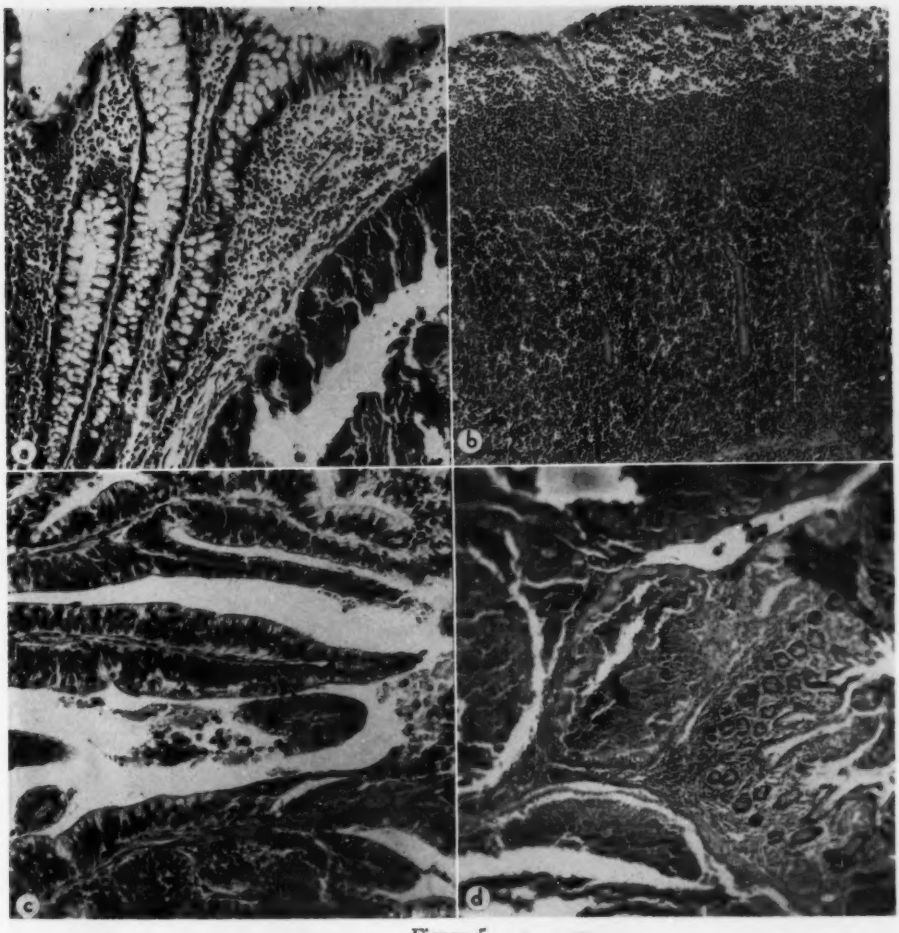


Figure 5

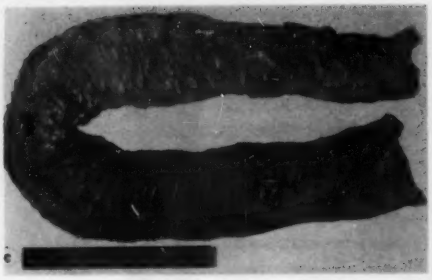
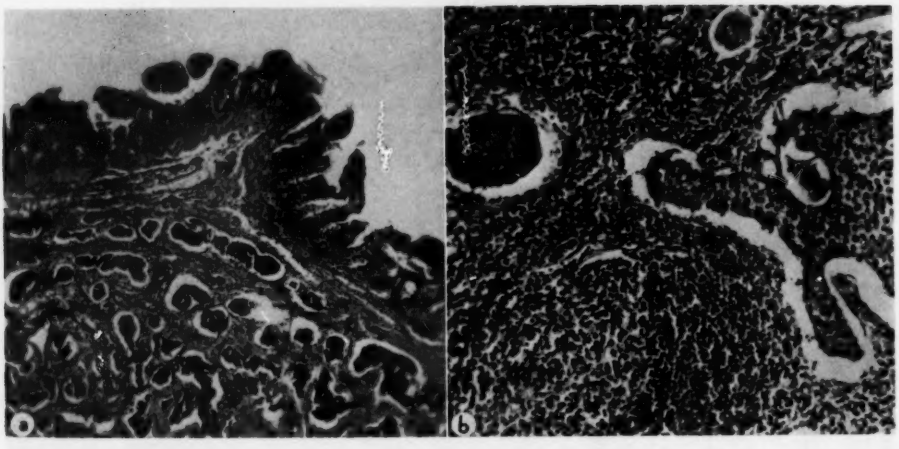
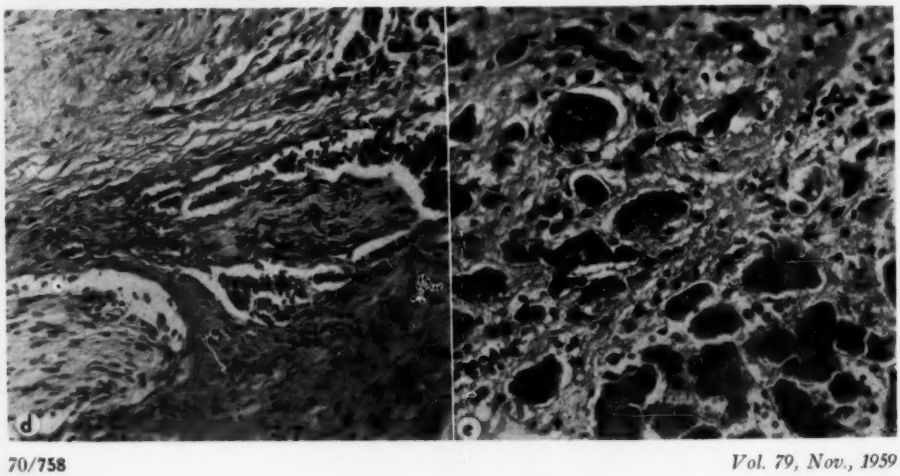


Fig. 6.—(*c*) Lymph node—metastatic "carcinoid"; reduced about 55% from mag. × 90. (*a*) Ileum—multicentric adenocarcinoma, so-called carcinoid. (*b*) Ileum—"carcinoid" with infiltration into the smooth muscle; reduced about 40% from mag. × 35. (*d*) Nerve—perineural lymphatic metastasis of "carcinoid"; reduced about 40% from mag. × 90. (*e*) Liver—metastatic "carcinoid"; reduced about 40% from mag. × 200.





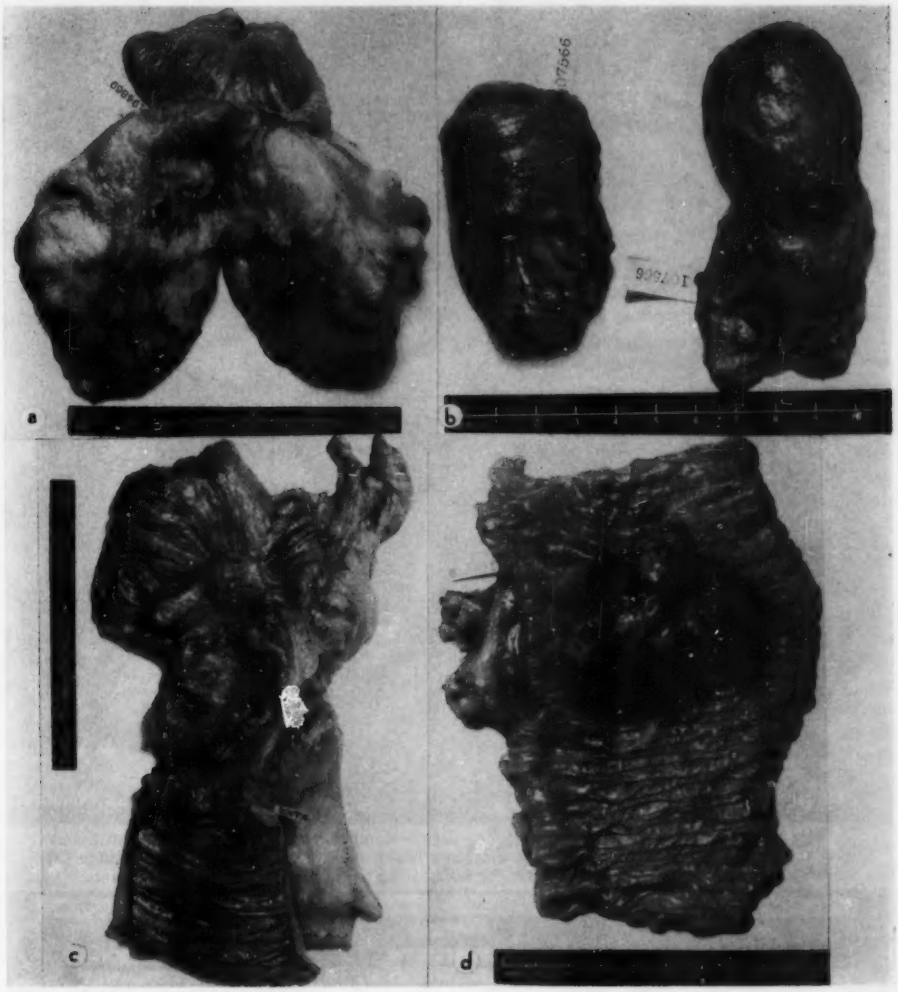


Fig. 7.—(*a*) Ileum—Grade I leiomyosarcoma which is undergoing some degeneration. (*b*) Ileum—neuroma of the wall of the ileum producing an intussusception. (*c*) Ileum—low-grade I infiltrating adenocarcinoma without involvement of regional lymph nodes. (*d*) Ileum—Grade II papillary adenocarcinoma without invasion of the wall of the muscle and without metastasis to regional lymph nodes.

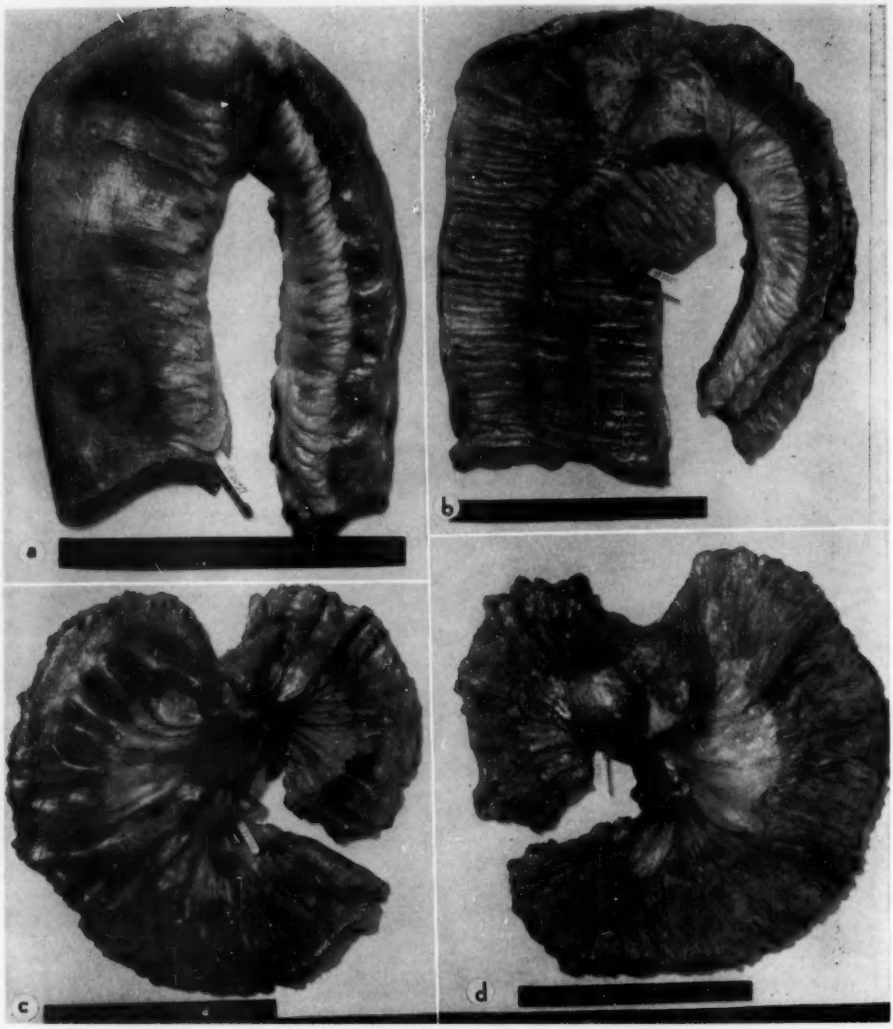


Fig. 8.—Moulage specimens. (*a*) and (*b*) Ileum—lymphocytic lymphosarcoma with extension into mesentery and involvement of a remote lymph node. (*c*) and (*d*) Ileum—Grade III adenocarcinoma with infiltration through the wall of the bowel and into the mesenteric fat.

ADENOCARCINOMA OF SMALL BOWEL		CARCINOMA OF AMPULLA		LYMPHOSARCOMA OF SMALL BOWEL	
31 CASES		17 CASES		22 CASES	
CLINICAL SYMPTOMS		CLINICAL SYMPTOMS		CLINICAL SYMPTOMS	
PAIN	30	PRURITUS	15	PAIN	22
WEIGHT LOSS	22	WEIGHT LOSS	15	WEIGHT LOSS	11
VOMITING	17	ANOREXIA	15	WEAKNESS	11
WEAKNESS	15	DARK URINE	14	CONSTIPATION	10
BLEEDING	11	WEAKNESS	14	DIARRHEA	9
CONSTIPATION	11	PAIN	12	VOMITING	9
DIARRHEA	7	VOMITING	9	BLEEDING	6
OBSTRUCTION	7	CHILLS AND FEVER	9	ANOREXIA	4
PHYSICAL FINDINGS		PHYSICAL FINDINGS		PHYSICAL FINDINGS	
ABDOMINAL TENDERNESS	21	JAUNDICE	16	PALPABLE MASS	15
PALPABLE MASS	13	PALPABLE MASS	10	ABDOMINAL TENDERNESS	13
ABDOMINAL DISTENTION	9	ABDOMINAL TENDERNESS	5	ABDOMINAL DISTENTION	4
ANEMIA	6	ABDOMINAL DISTENTION	2	JAUNDICE	3
JAUNDICE	4	ASCITES	1	NODES	1

Figure 9

A Study of Uropepsin as a Reflection of Gastric Secretory Activity

JAMES R. JUDE, M.D., and ALVIN H. HARRIS, M.D., Bethesda, Md.

Urine pepsinogen is a proenzyme with pepsin-like proteolytic activity in a highly acid substate. It was discovered by Brücke [2] in 1860 and confirmed by Grützner [6] in 1881-1882. The name, uropepsin, was originated by Bendersky [1] in 1890.

Pepsinogen is known to be produced by the chief cells of the gastric glands and secreted mainly into the gastric lumen, where, under the acid conditions present, it is autocatalytically converted into pepsin. A certain controversial portion is thought to be secreted as an endocrine function of the chief cells directly into the blood stream where it is carried to and excreted by the kidneys (uropepsin).

The proenzyme, pepsinogen, found in the urine, has been considered by some investigators to reflect closely the activity of the gastric mucosa. Others, however, have considered the relationship to be highly variable and inaccurate. On the basis that it is a constant one, many clinical studies have been performed to show how the readily collected urine can be of value as a diagnostic tool.

Only few of scores of research papers have attempted to prove the relationship of urine pepsin to gastric acid and pepsin. These have been under clinical circumstances which are not easily controlled. This study was undertaken in the dog to determine whether a correlation existed between gastric acid and pepsin and urine pepsin under a variety of control and experimental conditions.

Submitted for publication May 7, 1959.

Present address of Dr. Jude: The Johns Hopkins Hospital, Baltimore. Present address of Dr. Harris: University Hospitals of Cleveland, Cleveland, Ohio.

From the Surgery Branch, National Cancer Institute, National Institutes of Health, Public Health Service, U.S. Department of Health, Education, and Welfare.

Method

Four adult healthy female mongrel dogs weighing 35 to 50 lb. were used. A small Heidenhain pouch was created in each animal and a nylon cannula inserted and brought out of the upper abdomen for collection of gastric secretion. At the same or a subsequent operation, a similar nylon cannula was placed in the urinary bladder and brought out of the lower abdomen for collection of urine (Fig. 1), and the urethra ligated. Collections were made over consecutive 24-hour periods by attachment of modified rubber football bladders to the nylon cannulas. The animals were kept on their regular high-protein kennel diet after the immediate postoperative period. Control collections were begun two weeks after creation of the Heidenhain pouch and bladder cannulation, and continued for a period of 30 consecutive days. Control studies were performed on all four dogs. Two dogs were subsequently studied with daily histamine in yellow wax injections. They were given 30 to 60 mg. of histamine in the wax subcutaneously daily for periods of 8 and 17 days respectively. Intramuscular cortisone acetate was given to one dog over a period of 35 days in 50 to 200 mg. doses. After appropriate control periods, two animals were finally subjected to hypophysectomies by the parietal flap approach. The effect of the hypophysectomy on the parameters was evaluated after a rest period of two weeks.

The daily collected specimens of urine and gastric pouch secretion were refrigerated until analyzed in block units weekly. Repeated determination of test specimens so maintained failed to reveal any loss of activity over a two-week period of refrigeration of either urine or gastric pouch secretion.

Uropepsin was determined by the method of Sylvest [12] as modified by West, et al.[13] This method is dependent upon the conversion of paracasein to casein in a digest substrate of homogenized milk. The amount of pepsin present in the test sample

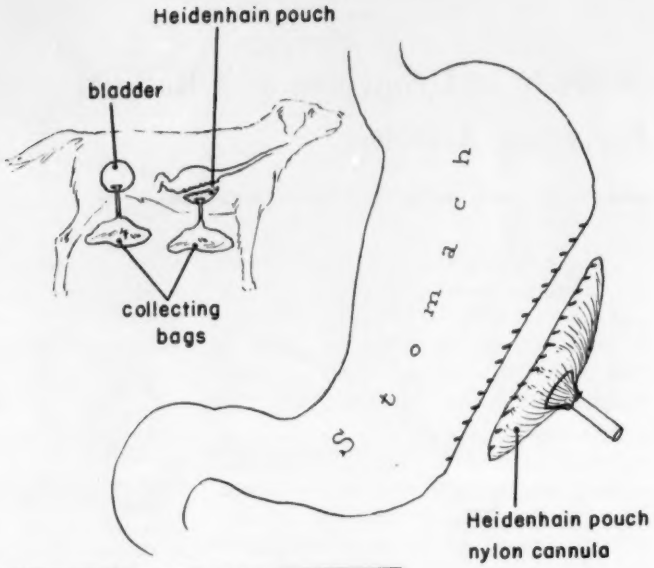


Fig. 1.—Diagram of Heidenhain pouch and urinary bladder with cannulas for collection as shown.

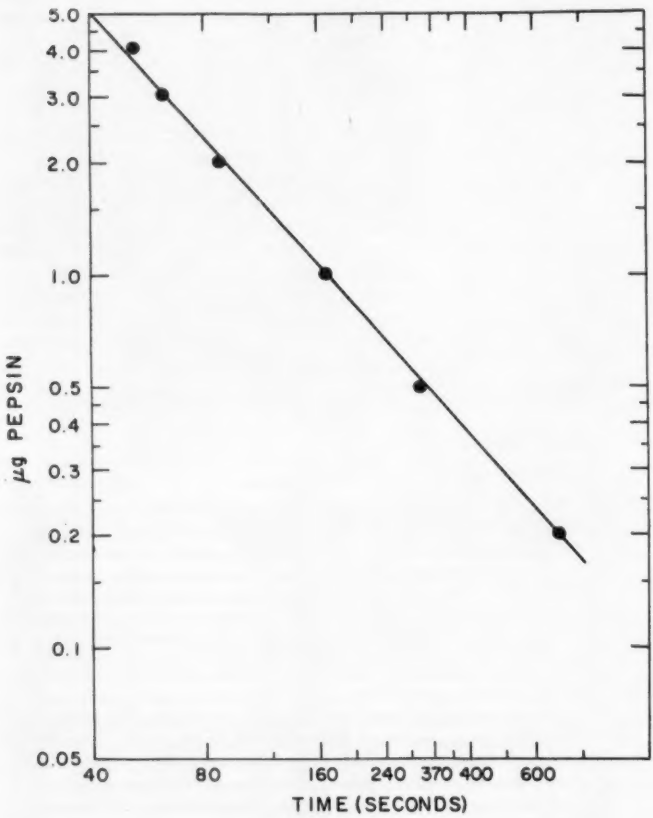
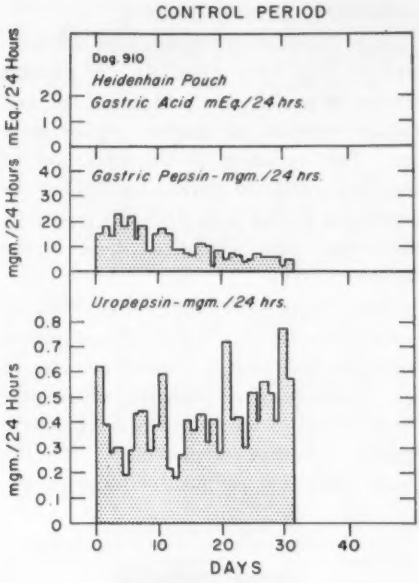


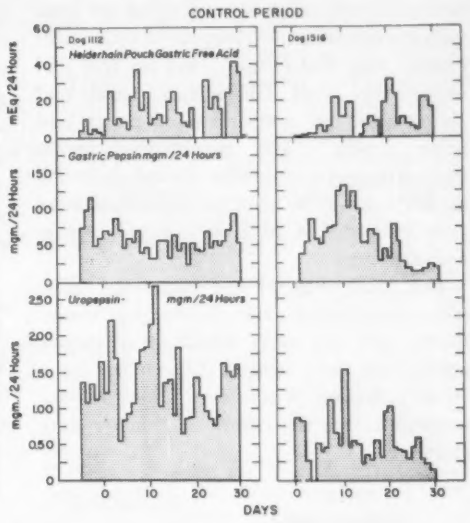
Fig. 2.—Standard pepsin curve (log-log scale).

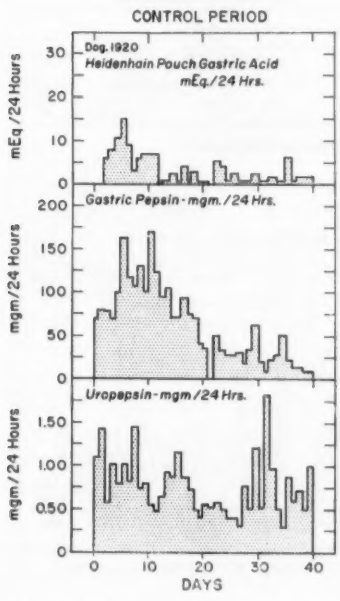
is determined from the time it takes to cause this reaction (precipitation). A control curve was determined with standard concentrations of pepsin (Fig. 2). The urine sample was diluted so that the time for precipitation fell in the range of 160 to 240 seconds. Results were expressed in milligrams of pepsin excreted per 24 hours.

Gastric pepsin was determined by the same method as the urine pepsinogen with employment of appropriate dilution. Results were expressed in milligrams secreted into the pouch in 24 hours.

Free Heidenhain pouch acid was determined by titration of an aliquot with 0.1 N NaOH to pH_3 with 0.5% alcoholic solution of dimethyl







Figs. 3, 4, 5.—Control curves showing daily corresponding gastric acid and pepsin, and uropepsin values for all four dogs.

aminoazobenzol (Topfer's reagent). Results were expressed in milliequivalents of free acid secreted in 24 hours.

Results

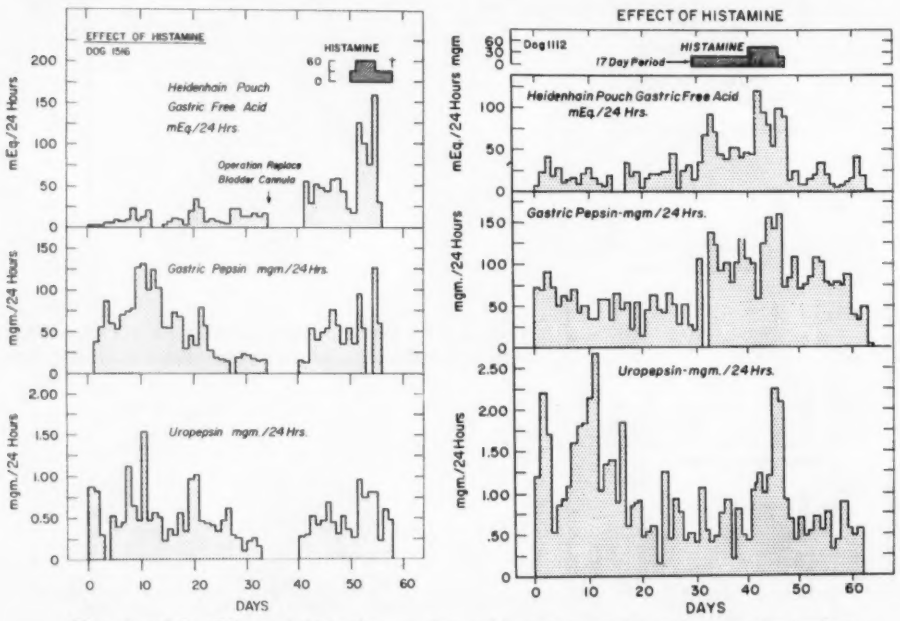
Figures 3, 4, and 5 show the day-to-day 24-hour excretion of Heidenhain pouch free acid and pepsin and urinary bladder pepsin in all four dogs during their control periods. Free acid is expressed in total milliequivalents and uropepsin in total milligrams. Dog 910 (Fig. 3) had no free acid in a very small Heidenhain pouch and shows only the comparison of pouch and urine pepsin. The maximum-minimum daily uropepsin excretion varied as much as 400% to 700%. Similar variations were seen in secretion of gastric pouch pepsin and free acid.

Dog 1920 (Fig. 5) had collections begun only several days after the surgical procedures, and the early elevation of pouch pepsin and free acid is thought to be a stress reflection of this fact. Note that the uropepsin did not show a similar early elevation.

Figures 6 and 7 show the effect of daily histamine. Changes in gastric pouch free acid occurred immediately as did pepsin. A brief late increase in uropepsin occurred in Dog 1112. Dog 1516 did not survive for a prolonged test. The control periods showed the marked daily variations in all parameters as previously noted.

Large doses of cortisone were administered to Dog 1112 (Fig. 8). A variable increase in gastric free acid and a late and gradual increase in gastric pepsin were seen. The variation in the excretion of uropepsin was quite marked throughout the observation period with pre- and postcortisone values very similar to those in the cortisone interval.

After hypophysectomy (Fig. 9), a marked decrease in pouch acid and pepsin production was seen. A sharp increase in these values occurred with the administration of small doses of cortisone given to support operative replacement of the urinary collection cannula. Uropepsin ex-



Figs. 6 and 7.—Effect of histamine on free acid, gastric pepsin, and uropepsin in dogs 1112 and 1516.

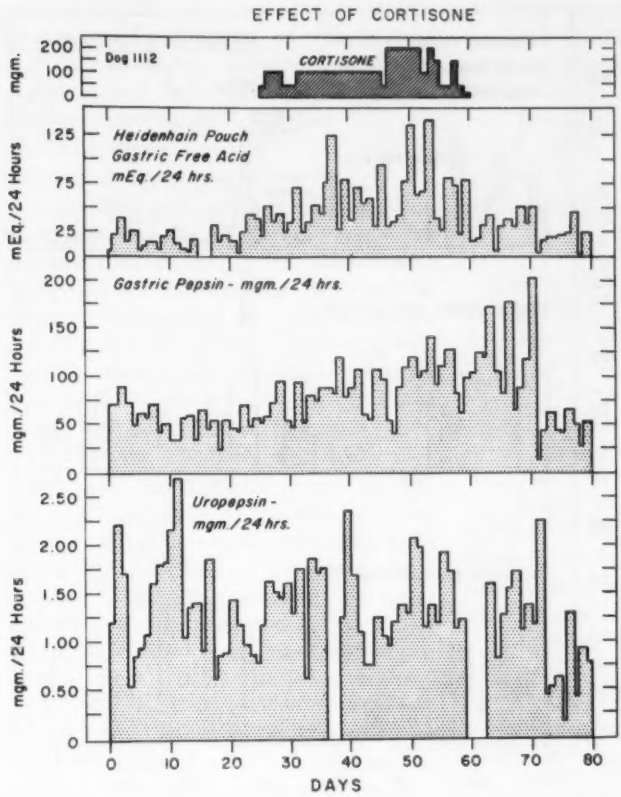


Fig. 8.—Effects of cortisone on free acid, gastric pepsin, and uropepsin.

cretion did not vary from the prehypophysectomy control collections.

Comment

The use of an experimental animal enabled close control of conditions under which the study was performed. From the Heidenhain pouch, daily total collections were obtained from a constant number of secreting gastric glands. These were under the same hormonal stimuli as the remaining stomach, and Heidenhain pouch secretion of necessity had to maintain a constant relationship to the parent stomach. Total urinary excretion was obtained from the bladder.

This experiment was designed to explore the questionable value of uropepsin as a clinical index of gastric mucosal secretory activity. From the control collection it was readily evident that a wide variation in day-to-day excretion occurred in all values. Most important was the completely independent variation of uropepsin excretion to pouch acid and pepsin excretion as shown by statistical analysis (Fig. 10). The daily value for gastric pepsin was plotted against uropepsin. For the concept to hold true, namely, that the uropepsin represents a constant fraction of the gastric pepsin, a straight line regression should be evident from the plotted parameters. This can be seen not to be the case. There fails to be any distinct regression either within each experimental group or between the groups. These facts point up the failure of uropepsin as an indication of gastric pepsin, for if the former does represent a

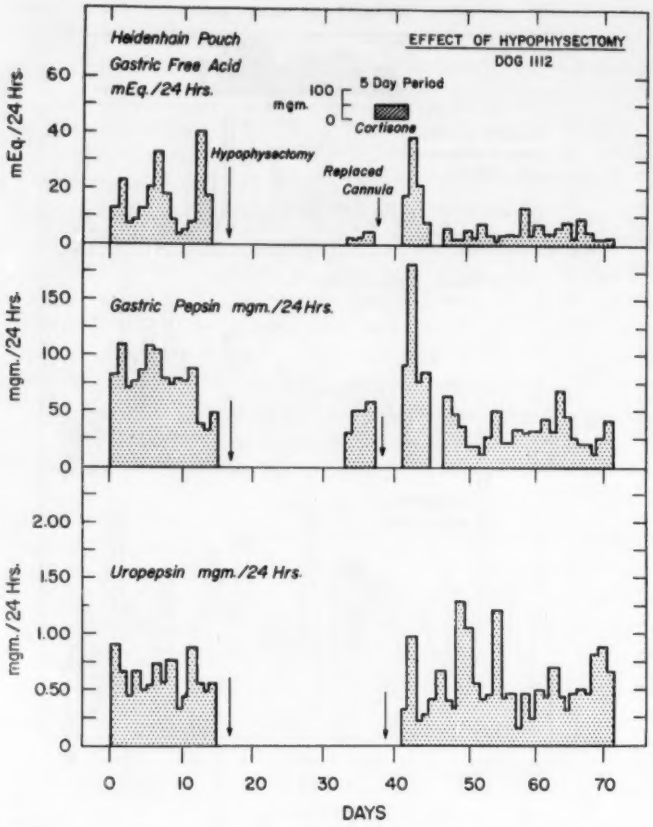


Fig. 9.—Effect of hypophysectomy on gastric acid, gastric pepsin and uropepsin.

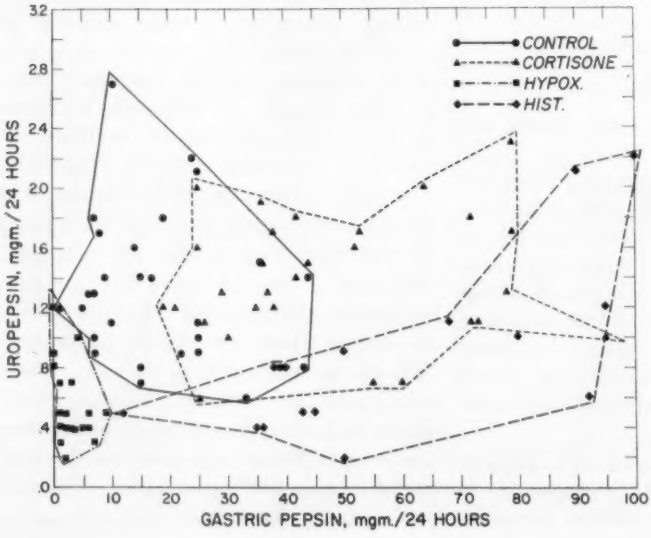


Fig. 10.—Schematic plot of daily uropepsin against corresponding gastric pepsin. Symbols for each phase of the experiment are as shown, with the different lines grouping the individual phases.

constant fraction of gastric pepsin output, as reported by Janowitz and Hollander,[8] and Gray et al.,[6] then changes in gastric pepsin should be consistently reproduced proportionately in the uropepsin. The plot of values shows variation in one with no constant change in the other.

It has been reported that cortisone stimulates gastric acid and pepsin production, and excretion of uropepsin.[4] The former are postulated to occur by way of the adrenalcortical-gastric axis, and the latter either by (1) an absolute increase in gastric pepsin production with the usual percentage being excreted into the circulation and then cleared by the kidney,[11] or (2) an increased renal clearance of plasma pepsin alone.[7]

We found that cortisone produced a definite augmentation in gastric acid and slow increase in gastric pepsin with delayed return to control levels of the latter. Daily variation in uropepsin excretion was great and there was no statistical correlation or significant trend. From these findings it must be considered that an inconstant percentage of pepsin is secreted directly into the plasma or cleared by the kidneys. Certainly the reported effect of cortisone increasing renal clearance was not seen.

Likewise, no statistical correlation was evident between gastric pouch acid and pepsin production and uropepsin excretion by use of the potent stimulator of gastric acid, histamine in beeswax. Sircus[10] had found a close correlation between the uropepsin output and the response distinct of the parietal cells to a triple dose histamine test. The absence of a relationship between gastric hyperacidity and uropepsin was, however, noted by Podore et al.,[9] Woodward,[14] and Bucher.[3] Any association between hyperacidity with increased pepsin secretion and increased uropepsin excretion must be considered fortuitous.

Complete hypophysectomy resulted in a decrease in both free acid and pepsin production. The stimulating effect of incidental cortisone on pouch acid and pepsin was in striking contrast to the lack of any effect on uropepsin excretion. The interruption of the pituitary-adrenalcortical-gastric pathway again gave indication of the absence of a direct effect of adrenocortical hormone on renal excretion of uropepsin or an indirect effect through the increase in gastric mucosal secretion of acid and pepsin.

Conclusions

Control studies gave strong indication of the lack of value of uropepsin excretion as a mirror of gastric mucosal activity in free acid or pepsin production. Considering that a strong change in gastric mucosal cellular stimulus might bring some order out of marked day-to-day variation, studies were performed to determine this possibility. Neither increased stimulation with injections of histamine in wax and large doses of cortisone or decrease in stimulation by ablation of the pituitary produced the expected corollary effect on uropepsin. It can only be concluded that in the experimental animal used no value could be given to evaluation of gastric mucosal activity in acid and pepsin production by study of uropepsin excretion. The wide variations noted also point up the danger in any single isolated determinations such as are frequently determined clinically. The variation of the recorded clinical results may reflect this but also appear to indicate the limited value of uropepsin determination in patients.

Summary

Uropepsin excretion was compared with simultaneously determined Heidenhain pouch free acid and pepsin secretion in four female mongrel dogs under (1) control conditions, (2) stimulation with histamine-in-yellow wax, (3) stimulation with cortisone, and (4) hypophysectomy.

A complete lack of statistical correlation of uropepsin excretion with either of the other two parameters was found in all circumstances.

The authors wish to express their appreciation to Dr. Jacob E. Lieberman, Biometrics Branch,

Division of Research Services, for assistance with the statistical data, and Dr. Delbert M. Bergenstal, Endocrinology Branch, National Cancer Institute, for his over-all assistance with this work.

Surgery Branch, National Cancer Institute.

REFERENCES

1. Bendersky, J.: Über die Ausscheidung der Verdauungsfermente (Pepsin, Trypsin, Ptyolin) aus dem Organismus bei gesunden und kranker Menschen, 121:554, 1890.

2. Brücke, E.: Die verdauende Substanz in Urin, Sitzungsb. k. Akad. Wissensch. Math.-naturw. Cl. 43:618, 1861.

3. Bucher, G. R., and Anderson, A.: The Uropepsin Output in Cats Given Histamine Caffeine in Beeswax, Fed. Proc. 7:16, 1948.

4. Gray, S. J.; Benson, J. A., Jr.; Reifenstein, R. W., and Spiro, H. M.: Chronic Stress and Peptic Ulcer, J.A.M.A. 147:1529, 1951.

5. Gray, S. J.; Ramsey, C. G.; Reifenstein, R. W., and Benson, J. A., Jr.: The Significance of Hormonal Factors in the Pathogenesis of Peptic Ulcer, Gastroenterology 25:156, 1953.

6. Grützner, P.: Über den Fermentgehalt des normal menschlichen Harnes, Breslau. Aertzl. Ztschr. 4:193, 1882.

7. Hirschowitz, B. I.: Significance of Increased Urinary Pepsinogen (Uropepsin) Excretion in Duodenal Ulcer and During ACTH Administration (Proceedings 29th Meeting Central Society for Clinical Research), J. Lab & Clin. Med. 48:817, 1956.

8. Janowitz, H. D., and Hollander, F.: Relation of Uropepsinogen Excretion to Gastic Pepsin in Man, J. Appl. Physiol. 4:53, 1951.

9. Podore, C. J.; Broh-Kahn, R. H., and Mirsky, I. A.: Uropepsin Excretion by Man: III. Uropepsin Excretion by Patients with Peptic Ulcer and Other Lesions of the Stomach, J. Clin. Invest. 27:834, 1948.

10. Sircus, W.: Studies of Uropepsinogen Excretion in Gastrointestinal Disorders, Quart. J. Med. 23:291, 1954.

11. Spiro, H. M.; Reifenstein, R. W., and Gray, S. J.: The Effect of ACTH upon Uropepsin Excretion, J. Lab. & Clin. Med. 35:899, 1950.

12. Sylvest, O.: Method for Determining Renninogen of Urine, Acta med. scandinav. 133: 289, 1949.

13. West, P. M.; Ellis, F. W., and Scott, B. L.: Simplified Method of Determining Excretion Rate of Uropepsin, J. Lab. & Clin. Med. 39:159, 1952.

14. Woodward, E. R.; Schapiro, H., and Armstrong, G.: Relation Between Uropepsin Excretion and Secretion of Gastric Juice, J. Appl. Physiol. 8:643, 1956.

Effect of Induced Infarction on Rat Liver Implanted with Walker Carcinoma 256

GUNTHER E. KRAUS, D.V.S., and ARTURO BELTRAN, M.D., Buffalo

Ligation of a branch of the portal vein or of an extrahepatic bile duct results in atrophy of the corresponding liver lobe. The remaining liver undergoes compensatory hypertrophy. This process is well tolerated by rabbits and dogs.[1,4,5] Complete devascularization of a portion of the liver results in infarction. When necrotic parts of liver tissue are left within their abdomen, dogs die within 36 hours. There is evidence that death occurs only if the liver tissue becomes decomposed by bacterial action.[2] Rats, however, are able to control massive bacterial growth in necrotic liver tissue and survive infarction of up to 70% of their liver (100% of 18 rats[3]).

If ligation of various structures of the portal hilus, leading either to atrophy or to necrosis of part of the liver, is followed by regression of a malignant growth within the affected liver tissue, this method could be used as a conservative surgical treatment of carcinoma of the liver that is confined to only one lobe. The present study deals with an investigation of this basic concept.

Materials and Methods

Wistar rats of both sexes, 6 to 8 weeks old, were used. The animals were anesthetized with 40-50 mg/kg. of pentobarbital sodium by intraperitoneal injection. The abdomen was opened by a midline incision to expose the liver.

The rat liver consists of three leaf-shaped diaphragmatic lobes, a right caudal lobe, a caudate process, and one or two omental processes. There is no gallbladder. Ramifications of the portal vein and the bile duct are extrahepatic in position.

Submitted for publication April 23, 1959.

Department of Experimental Surgery, Roswell Park Memorial Institute.

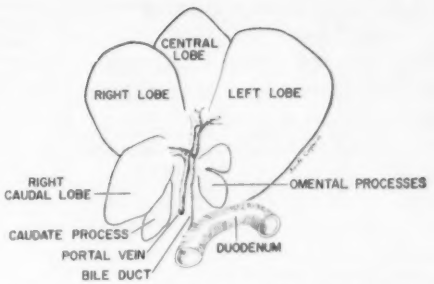


Fig. 1.—Visceral surface of rat liver and porta hepatis.

Each lobe is supplied by one or more branches of the hepatic artery (Fig. 1).

For portal exposure the diaphragmatic lobes were delivered through the incision and retracted. Either the lobar bile duct, or the branch of the portal vein, or all structures leading to or from the right caudal liver lobe were prepared by blunt dissection and ligated. The abdomen was closed in two layers.

Walker carcinoma 256 was used for implantation into the liver. The tumor was grown subcutaneously in the flanks of rats for two weeks. For transplantation it was cut into pieces of approximately 0.5×0.5 mm. and moistened with Ringer's solution. The abdomen of rats to be implanted was opened along the right costal arch. A piece of tumor was blotted dry on sterile gauze to avoid tumor-cell contamination of the peritoneum. It was then inserted into the right caudal liver lobe with a closed hemostat. Sealing of the stab wound was accomplished by gentle pressure with a sterile gauze sponge.

The experiments were divided into three groups. In the first group all three modes of ligation were applied to a total of 40 rats (control ligations); in the second group tumor was implanted into the right caudal liver lobe in 40 rats (control implantations); in the third group tumor implantation into the right caudal liver lobe in 56 rats was followed by the three types of ligation after one week (ligations of tumor implanted lobes). To avoid repetitions the detailed experimental plan is given under results (see also Table).

Summary of Procedures and Results

Group	No. of Rats	Implantation of Walker Carcinoma into RCL *	Type of Ligation	Remarks on Pathology	When Killed	No. of Animals with Tumor Regression	Per Cent of Tumor Regression
I	13	No	Bile duct from RCL	Atrophy, followed by restitution	Weekly in groups of 2 each	--	--
	12	No	Portal venous branch to RCL	Slowly progressing atrophy	Weekly in groups of 2 each	--	-
	15	No	Bile duct, hep. art., and portal venous branches of RCL	Lobar infarction with subsequent encapsulation	Weekly in groups of 2 each	--	--
II	23 †	Yes	No	Massive tumor growth with spread by contact and via lymph channels	--	0	0
	10 †	Yes	No	(See text)	Weekly in groups of 2 each	0	0
III	12	Yes	Bile duct from RCL †	--	--	2	16.6
	16 §	Yes	Portal venous branch to RCL ‡	--	--	5	31.2
	19	Yes	Bile duct, hep. art., and portal venous branches of RCL ‡	--	--	14	73.7

* RCL=right caudal liver lobe.

† Number of animals includes those animals only that showed tumor growth one week after implantation, confirmed by exploratory laparotomy.

‡ Ligation was done one week after tumor implantation.

§ There were originally 20 animals, 4 of which developed liver infarct following ligation with regression of the tumor. Only the remaining 16 rats are shown on this table.

Part (Table) of the animals were killed by placing them in a chloroform jar at weekly intervals of from one to six weeks in order to establish the course of pathological events. Others (Table) remained alive, until spontaneous death occurred. All rats were autopsied, and representative specimens were fixed in 10% buffered formalin for histological examination. Sections were stained with hematoxylin-eosin.

Results

I. Control Ligations.—In 13 rats the bile duct from the right caudal liver lobe was ligated. The animals were killed in groups of two each at weekly intervals. During the first two weeks after ligation the right caudal lobe appeared mottled, lighter in color, and softer. Its size was slightly decreased. On gross inspection three or more weeks after ligation, a normal right caudal lobe was found, sealed by adhesions to other lobes or to the duodenum. Histological examination showed minute deposits of bile pigment within and around the portal triads. Groups of round cells were seen either in the interstitial tissues or taking the place of missing liver cells. There was no proliferation of bile ducts. From the third week on the histological picture was almost identical with normal liver. The failure of the affected lobe to develop progressive atrophy and early signs of biliary cirrhosis points to a possible reconstruction of the bile duct. This interesting phenomenon has previously been observed after ligation of the common duct of rats.[6] The patency of the duct that was ligated was not examined in the present study.

In 12 animals the branch of the portal vein to the right caudal lobe was ligated. Two rats each were killed at weekly intervals. After one week the lobe appeared darker with light tan mottling. A more uniform tan color was seen after two or more weeks. The lobe gradually decreased in size during the six weeks of observation. Microscopical examination showed some dilatation of the sublobar and central veins and occasionally hemorrhages into the scarce connective tissue of the portal triads. Scarring of minor degree was noted later on. Minor subcapsular bleeding was fre-

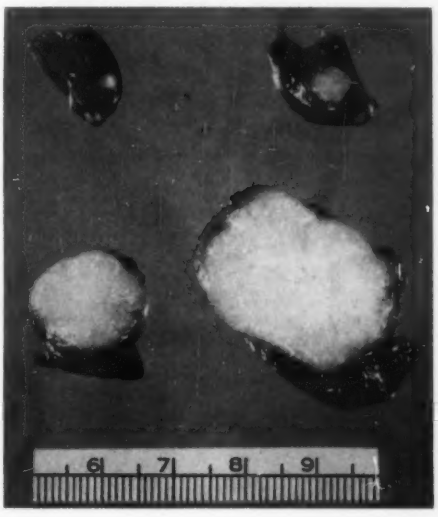
quently seen. The liver cells became smaller. Bile pigment occurred in the form of deposits within the portal triads from the fourth week on.

In 15 rats all structures of the hilus leading to or from the right caudal lobe were ligated. All the animals remained alert and apparently healthy during a survival period of from one to four weeks. No antibiotic drugs were given. After one week the infarcted lobe was soft and yellow, with subcapsular hemorrhages. Its size was normal or even enlarged. During the second to the fourth week the lobe shrank, became harder, and took on a more globular shape. Its capsule became thicker and of a dirty yellow color (Fig. 2). Histologically the classical signs of infarction were observed: The liver tissue underwent coagulation necrosis; it stained homogenously red with hematoxylin-eosin stain, and retained clearly the structural features of the lobules. The nuclei appeared as faint, ghost-like structures, with little, mostly marginated chromatin. After one week the lobe was surrounded by granulation tissue. Leukocytes formed a dense zone of demarcation at the periphery of the necrotic liver tissue. Later on the fibrous components of the capsular tissue increased to form a thick capsule of mature fibrous tissue. Giant cells were sometimes present. Bile-duct epithelium proliferated extensively in the broader parts of the capsule, forming irregular groups or ducts of various sizes. At the fourth week a fairly firm capsule was separated from the necrotic liver tissue by a layer of purulent exudate, consisting almost solely of polymorphonuclear leukocytes. At this time an unusual number of thick-walled arteries could be seen within and on the peritoneal surface of the fibrous capsule. A tendency toward separation of the dead lobe mass into subdivisions was seen; leukocytes, followed by granulation tissue invaded at several points from the periphery centripetally in a radial fashion.

II. Control Implantations.—In 40 rats tumor was implanted into the right caudal lobe. The take rate was 82.5% as determined by exploratory laparotomy and autopsy of succumbed or killed animals. Seven rats without tumor growth were excluded from the experiment. All 33 rats in which the tumor grew succumbed to the invasion by tumor. No spontaneous regression was observed. Metastatic spread was studied by weekly killing of two animals each. The animals developed a distended abdomen, clearly visible from the third or fourth week on, which was caused by the tumor nodules and ascitic fluid. Type or

Fig. 2.—Diaphragmatic face of liver with infarcted right caudal lobe. Subcapsular hemorrhages are visible.

Fig. 3.—Walker tumor in liver one, two, three, and four weeks after implantation.



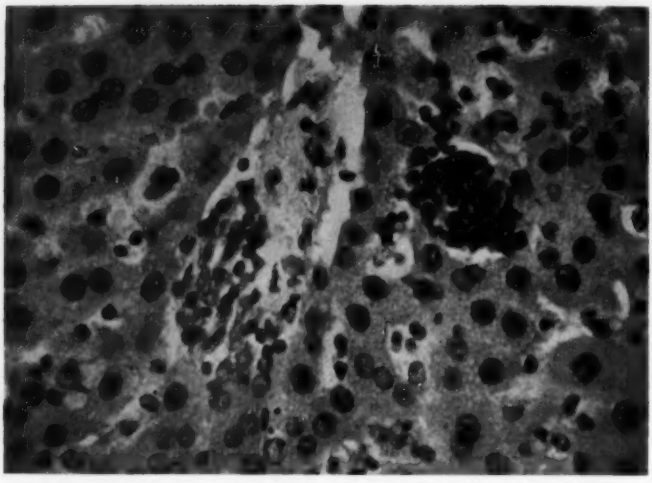


Fig. 4. — Photomicrograph of liver showing two areas of invasion of tumor cells infiltrated with lymphocytes.

etiology of this ascites was not studied. The average survival time of 23 animals was 37 days.

Weekly killing of two animals each showed the tumor to be 2 to 4 mm. in diameter after one week, 5 to 10 mm. at the end of the second week. Metastatic nodules in other lobes of the liver occurred from the third week on (Fig. 3). Lymphatic spread was seen in the hepatic ligaments with frequent massive growth in the area of the adrenal glands, in the mesentery, and, by direct extension through the adhesions formed, in the ventral abdominal wall. No gross metastasis was detected in the lung. Hemorrhage into the capsule of tumor-bearing liver, and necrosis in the center of larger nodules were always present. The ascitic fluid was usually of serosanguineous character. Histologically the tumor invaded the liver by direct infiltration. Islets of tumor cells within liver parenchyma were seen, usually together with lymphocytes (Fig. 4). Normally staining heaps of liver cells were found scattered throughout the tumor (Fig. 5). Random examination of lung tissue revealed no microscopic tumor metastases.

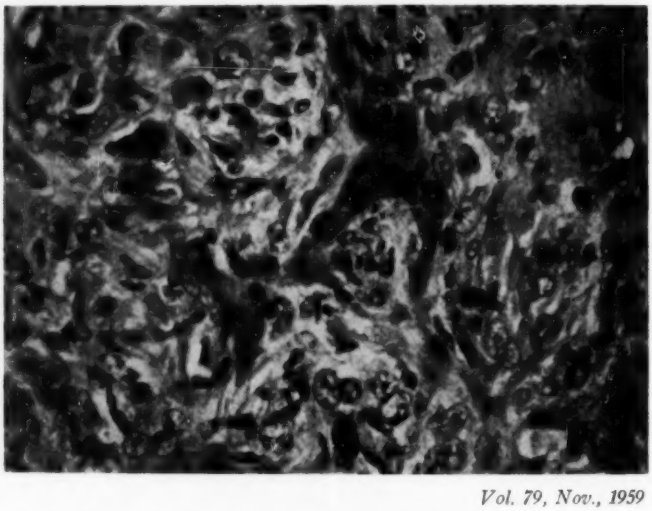


Fig. 5. — Photomicrograph of Walker tumor growing in the liver. A group of normal staining liver cells is visible.

III. Ligation Following Tumor Implantation.—Tumor was implanted into the right caudal lobe of 56 animals, followed by an exploratory laparotomy one week later. In five animals no growth of the implant was seen; they were discarded. In the remaining 51 rats nodules 2 to 4 mm. in diameter were encountered. Adhesions had formed between the implanted lobe and the abdominal wall, the duodenum, and other liver lobes. These were gently severed. The 51 animals underwent ligations at this time. In 12 cases the bile duct to the tumor-bearing liver lobe was ligated; in 20 cases the analogous branch of the portal vein, and in 19 cases all hilar structures of the right caudal lobe.

After the ligation of the bile duct in 12 rats 10 animals succumbed, owing to massive tumor growth. The two remaining animals were killed 43 and 58 days after tumor implantation. There were adhesions to neighboring structures, but no evidence of tumor on gross or microscopical examination.

Ligation of the branch of the portal vein to the implanted liver lobe in 20 rats yielded progressing tumor proliferation and death in 11 animals. Nine animals were apparently healthy six weeks after the tumor had been implanted. Their killing in the seventh and eighth week showed that the tumor had regressed. In four of these animals infarction was found; possibly the arterial branches to the right caudal lobe had been injured at the time the adhesions were severed surgically. These four animals were excluded from the study. Hence only in 5 animals out of 16 can the atrophy, induced by depriving the lobe of its portal blood supply, be considered the basis of the failure of the tumor to grow.

Among 19 rats in which infarction was produced by ligation of all hilar structures leading to the right caudal lobe, 5 animals died from extensive tumor growth. Fourteen rats were killed in an apparently healthy condition seven to eight weeks after the tumor had been implanted. Tumor was detected neither grossly, nor on microscopical examination. The right caudal lobe was transformed into a hard, small nodule of creamy color.

Comment

Bile-duct ligation was followed by temporary changes only of the affected lobe in the direction toward atrophy. Recovery of the liver tissue occurred. An explanation could be found in the possibility of spontaneous reconstruction of the bile duct.[6] The percentage of tumor regression was 16.6% in these rats in which tumor had been implanted.

Ligation of the portal venous branch led to atrophy which developed slowly without recovery of the affected liver parenchyma. In rats with tumor implanted lobes this type of ligation was associated with 31.2% regression of the tumor.

Infarction of the lobe by mass ligation of the respective portal radicle developed rapidly. In tumor-implanted rats regression of the neoplasm was accomplished in 73.7% with this type of treatment.

By comparison of the results certain conclusions can be drawn. Because the tumor controls never regressed spontaneously, and those animals not showing tumor growth at the time of ligation were excluded from the study, the regression of tumor following the various types of ligation is directly related to the various pathological processes induced by the ligations. It appears that the extent and the rapidity of the process induced by ligation plus other factors, such as collateral circulation, determine the final fate of the tumor.

Bile-duct ligation with very insignificant liver changes of short duration probably allows the tumor an excellent chance to survive. The process of atrophy after portal-vein ligation runs a slow course, which is certainly surpassed by the rate of tumor proliferation. Therefore the tumor still has a relatively great chance to withstand this minor crisis. The quick-striking infarction, produced by ligation of

the entire lobar hilar structures, permits survival of tumor in the minority of cases only. One would not at all expect survival of tumor that is embedded in necrotic liver tissue. A logical explanation for that is offered by the observation that sometimes the implant extends to the surface of the liver after one week of proliferation. The accessibility of peritoneal fluid and the proximity of vascular adhesions to the neoplasm may then be decisive factors, preventing death of a sufficient number of tumor cells for further tumor proliferation.

The rat is known to withstand wound contamination very well. In our study this species was able to survive lobar liver infarction without any morbidity. There was no bacterial decomposition of the necrotic liver parenchyma, which has been shown to lead to death within 36 hours in the dog.[2] Instead the rat answers the injury by encapsulation and slowly progressing organization of the infarct. The favorable results of liver infarction in the treatment of liver tumor and the complete absence of alarming signs after infarction is induced in the rat invite studies of similar character in species other than the rat.

The small number of animals used for each group does not permit a direct adoption of the results for an evaluation of the methods in regard to their therapeutic use.

Summary and Conclusion

Ligation of the bile duct to one liver lobe in the rat results in temporary atrophic changes, while ligation of the concomitant portal vein induces irreversible atrophy. When all structures of the portal radicle to a liver lobe are ligated, infarction with subsequent encapsulation is produced; such infarction is compatible with the animal's life.

Walker carcinoma, implanted into one liver lobe, leads to death of the rat in an average time of 37 days.

Bile-duct ligation of the tumor-implanted lobe results in 16.6% regression of the tumor, while similar ligation of the portal vein radicle gives a regression rate of 31.2%. Infarction prevents tumor growth in 73.3% of rats with Walker carcinoma implanted into a liver lobe.

The authors wish to express their thanks for the technical assistance of Mrs. Theresa Bittner.

Roswell Park Memorial Institute.

REFERENCES

1. Beltran, A.; Kraus, G. E., and Simpson, C. L.: Lobar Liver Atrophy Following Ligation of Bile Ducts, A.M.A. Arch. Surg. 78:380 (March) 1959.

2. Ellis, J. Z., and Dragstedt, L. R.: Liver Autolysis in Vivo, Arch. Surg. 20:8 (Jan.) 1930.

3. Kraus, G. E.: The Tolerance of Animals Toward Liver Infarction, unpublished data.

4. Rous, P., and Larimore, L. D.: Relation of the Portal Blood to Liver Maintenance: A Demonstration of Liver Atrophy Conditional on Compensation, J. Exper. Med. 31:609 (May) 1920.

5. Schalm, L.; Bax, H. R., and Mansens, B. J.: Atrophy of the Liver After Occlusion of the Bile Ducts or Portal Vein and Compensatory Hypertrophy of the Nonoccluded Portion and Its Clinical Importance, Gastroenterology 31:131 (Aug.) 1956.

6. Trams, E. G., and Symeonidis, A.: Morphologic and Functional Changes in the Livers of Rats After Ligation or Excision of the Common Bile Duct, Am. J. Path. 33:13 (Jan.-Feb.) 1957.

The Prevention of Primary Postoperative Thrombosis

A Reliable Capillary Tube Clotting Time Method

H. F. McNICKLE, F.R.C.S. (Eng.), Auckland, New Zealand

I have personally done many hundreds of capillary tube clotting time estimations, using homemade glass capillary tubes of a certain size. Gradually, by trial and error, and by chance, ways have been found to reduce or eliminate some of the variables in the test. Unexpectedly, one of the most important variables was found to be in the capillary tubes themselves. This led to a study of the behavior of homemade capillary tubes when used to test the clotting time of normal blood at body temperature, and to the observation, many times repeated, that freshly drawn capillary tubes give short and erratic clotting times, but that tubes from the same batch, after being allowed to age for some months, give very uniform and dependable clotting times, and continue to do so indefinitely. It was also possible to demonstrate that there is only one normal clotting time for a given set of properly prepared and aged capillary tubes.

The next step was to use these reliable capillary tubes on patients undergoing major surgery, in an effort to predict and forestall primary postoperative thrombosis and embolism. Such an investigation was begun in the second half of 1948 and is still continuing. It has proved to be a fascinating and rewarding study.

Capillary Tube Method

Making the Tubes.—All capillary tubes were drawn from ¼ in. soda glass tubing. The tubing tends to vary somewhat in composition, in diameter, and in wall thickness. The tubing required was selected from a single bundle to ensure as far as possible that the glass used for a batch of capillary tubes was of uniform composition. Tubing from 6 to 6.5 mm. outside diameter and running about 36 ft. to the pound was preferred, because capillary tubes made from it usually showed the phenomenon of "beading" well, and were easily nicked by a sharp file. Thin-walled tubing was not suitable because capillary tubes made from it were so thin-walled that the file tended to crush them or to cut right through them. On the other hand, thick-walled tubing was found to be unsuitable because capillary tubes drawn from it were thick-walled too. The repeated heavy filing of such tubes in order to break off successive segments causes much unnecessary disturbance of the contained blood.

The tubing was washed inside and out in warm weak Teepol solution (a solution of sodium secondary alkyl sulfates), rinsed for a long time in running tap water, and finally rinsed with distilled water. Tubing was either pulled as soon as it was dry or else was loosely capped with cellophane at each end and wrapped to exclude dust.

The capillary tubes were drawn by hand by heating segments of tubing over a fishtail burner and drawing them out to arm's length. From the long capillary tubes thus formed sections of 1 mm. outside diameter were selected, were cut into 3 cm. lengths (not 3 in. lengths), and were stored in a clean, dust-proof, clear glass container labeled with the date of manufacture. Clean rubber gloves were worn during pulling and cutting to exclude perspiration. These tubes are considerably smaller than those generally advocated but were found to be quite adequate and to offer definite advantages.

Submitted for publication April 23, 1959.

Aging the Tubes.—It is a definite fact, which I have proved repeatedly, that glass capillary tubes improve with keeping. At first, when freshly drawn, they give short and somewhat erratic clotting times, but after a period of aging they give longer and very consistent clotting times. This observation is of great importance to all who use the capillary tube method, and has implications for others who study blood coagulation in vitro. A few words about the properties of glass will make this clearer.

First of all, blood in a glass container inevitably clots, the time taken being as much a property of the container as of the contained blood. A glass surface is fairly active in promoting coagulation compared with, say, glass that has been coated with silicone or paraffin, and it must be remembered that in a capillary tube a small quantity of blood is in contact with a relatively large area of glass. In a 1 mm. diameter tube this is equivalent to a film of blood 0.25 mm. thick spread on glass, or to a film of blood 0.5 mm. thick between two glass surfaces.

Secondly, it must be realized that heating glass to somewhere near its melting point profoundly alters its surface properties and for a long time. For example, if one heats one end of a clean glass slide greatly, allows it to cool completely, and then breathes on the glass, one finds that the condensation of moisture causes minimal frosting at the end which had been heated and dense white frosting at the other end. This "breath figure" is apparently due to a greatly increased wettability of the heated end, for under low magnification it can be seen that moisture has indeed condensed at the heated end, but is in much larger and flatter droplets. Also if the slide is immersed in water and removed, it will be noticed that the water on the surface of the end which has been heated clings to the glass in a uniform film instead of gathering itself into droplets as it does at the other end. This breath figure and increased wettability remain for many months, but can be reversed by boiling in distilled water for one hour, or by autoclaving for 20 minutes at 15 lb. pressure. However, capillary tubes are not aged artificially by boiling or autoclaving for this length of time, thus showing that some surface property other than wettability is also involved.

All batches of tubes were allowed to age naturally until they gave a clotting time of 7 minutes or longer when used on normal patients. They were then considered to be ready for general use. The minimum aging time was at least nine months when tubes were stored in a clear glass box standing on the desk in diffuse daylight. If the tubes remained on the desk after this, the aging process still continued but at a very reduced rate, a clotting time of 9 minutes or better being reached after two years or more. During the whole of this time the tubes behaved in a strikingly uniform manner, giving the same clotting time when the test was repeated on the same patient and, with few exceptions, giving the same, or nearly the same clotting time (within a minute either way) on consecutive patients tested before operation. Figure 1 is an attempt to show graphically how tubes behave more uniformly as aging proceeds.

During aging, the recovery of glass, or at least of its surface properties which affect coagulation, may be likened to the decay of a radioactive substance.[2] Figure 2 is an exponential decay graph assuming arbitrarily a half-life of three months. The

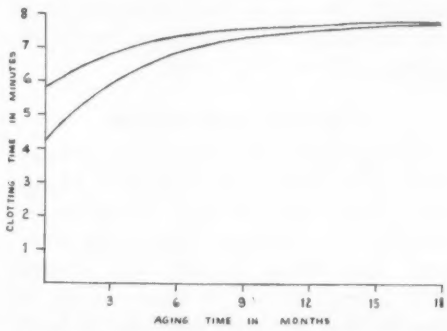


Fig. 1.—Graph to show how clotting times improve as capillary tubes age in diffuse daylight.

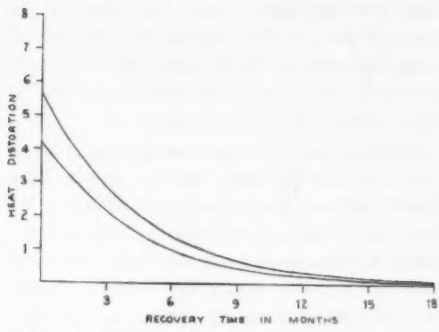


Fig. 2.—Exponential decay graph assuming a half-life of three months.

glass would recover by half in the first three months, by another quarter in the next three months, by an eighth in the third three months, and so on; also the differences between individual capillary tubes would tend to disappear at the same rate.

When tubes were stored in the dark in a metal box the aging process was greatly retarded, at least 20 months elapsing before the tubes became reliable enough to use. On the other hand, exposure to sunlight greatly accelerated the aging process. Freshly drawn tubes stored in a clear glass container in a glass house were ready to use after only nine weeks of average autumn sunshine (latitude 37 degrees). Strangely enough, rapid aging by this method appears to be possible only if the tubes are exposed to sunlight soon after their manufacture. Ready-made tubes of uncertain age cannot be expected to behave in this manner.

Other Equipment.—This includes a straight, triangular-pointed, stainless steel needle or a glass bayonet to puncture the finger. The needle is conveniently mounted in the rubber stopper of a small bottle containing 95% alcohol (not emetine spirit) so that the needle point is in the alcohol.

Since the test is to be conducted at or near body temperature, some means of keeping the capillary tube warm has to be provided. A simple piece of equipment, and one which can be carried to the bedside, is a brown glass, hexagonal, 8 oz. bottle of the type which has longitudinal ridges on two of its sides. The bottle filled with water at 100 F is laid on its side, and the capillary tube is laid in one of the grooves. The bottle loses 2 F in five minutes at a room temperature of 72 F.

A stop watch is unnecessary. Even a second hand is not essential, if the watch has a large enough dial with clear markings.

Preparing the Finger.—If the patient's hand is perspiring, it should be held under the cold tap for a minute and then dried. In the case of a bed patient a clean, cold, wet face cloth may be used to sponge the hand and may be given to the patient to hold in the palm. If the hand is cool and dry, this step is unnecessary.

Needle and stopper are removed from the alcohol bottle and are stood upright to dry. The dorsum of the terminal phalanx of the index finger is swabbed with alcohol and the excess is removed with cotton wool. Half a minute is allowed for the needle and finger to dry.

Filling the Capillary Tube.—The site for the skin puncture is chosen close to the nail fold and to one side of it. The skin there is reasonably thin and not too sensitive. The finger should be relaxed because active flexion sometimes empties the capillaries of the nail fold. The operator encircles the patient's finger with his own left index finger and thumb and quickly milks the blood toward the finger tip. With his right hand he makes the skin puncture, lays down the needle, picks up the capillary tube and holds it to the drop of blood in a horizontal or slightly downhill position.

Certain points of technique need emphasis. Firstly, the puncture must be made boldly so that the blood will well out quickly. Light pressure on the pulp, if it accelerates the blood flow, does not materially affect the clotting time, but heavy squeezing is not permissible because tissue juice is expressed with the blood and clotting is accelerated. This has been emphasized repeatedly. It is best to avoid squeezing altogether. This can be done quite easily

by using a very sharp glass bayonet and by making a second puncture at once if the first puncture does not bleed immediately. Secondly, the blood should not remain in contact with the finger a moment longer than necessary. Thirdly, if the drop expressed is insufficient to fill the tube, a second drop from the same puncture must not be used. The second drop always clots faster than the first one. It will be appreciated that the small-sized capillary tubes used in this study, requiring as they do much less blood to fill them, reduce to a minimum the need for squeezing, the time the blood is in contact with the finger, and the time taken to fill the tube. These effects are cumulative. The tube should be full within 6 seconds of the needle puncture; 5 seconds is average.

Incubating the Tube.—The end of the tube which was held to the finger is wiped clean and the tube is laid in a groove on the side of the warm bottle. Since the blood in the tube always clots first in the end of the tube which was held to the finger (the end of the tube that the blood entered), the tube is laid on the bottle with that end always pointing in the same direction, say to the left.

In cool weather a little hot water has to be added to the bottle after four or five minutes, or, better, a second bottle freshly filled with water at 100 F is substituted for the first. One soon becomes expert at judging the temperature of the bottle without a thermometer. A freshly filled bottle should feel just warm on the cheek, and bottles should be changed as soon as the warmth becomes less perceptible. This method may seem crude but it works well in practice. Actually, the temperature control can be just as accurate as the operator cares to make it.

Beading.—Homemade capillary tubes usually have an unevenness in the wall which acts like the lens front of a clinical thermometer. The column of blood in such tubes can be seen to become first ragged and then definitely beaded some time before clotting takes place. This beading always begins at the end of the tube which was held to the finger (the end the blood entered), and proceeds slowly along the tube toward the other end.

Beading is best seen when the tube is held horizontally and rotated slowly in a good diffuse light near a window, but against a dark background, such as the window sill, until a broad light reflex is seen. It is in this light reflex that the shaggy outline and the beading appear. Direct sunlight and electric light cause rather much reflection from the surface of the glass. If tests have to be performed at night they are best done under the shadowless operating lamp.

Capillary tubes drawn from tubing of proper weight show the phenomenon clearly and regularly, the beading beginning at say 4 minutes and being pronounced at 5 minutes. The importance of the "beading time" is that it is a rough guide to the clotting time; if the beading time is short, the clotting time will be short and vice versa. Again, since beading always occurs some time before actual clotting takes place, one can safely postpone the cutting of the tube until beading is well advanced, and so avoid unnecessary disturbance of the contained blood.

Cutting the Tube.—Since the blood always clots first at the end of the tube the blood entered, this end is chosen for cutting. A nick is made in the glass ⅛ in. from the end of the tube by drawing a sharp file slowly across it until it is felt to bite in. Then, with the tip of the right thumbnail squarely behind the nick, the tube is bent over the nail until it breaks. If this has been done carefully, the two fragments will still be in contact. They are then separated slowly in a good light and against a smooth white background. Cutting is repeated until a fine thread of clot is seen as the fragments are separated. As soon as this thread is seen, cutting is begun at the other end of the tube, the end opposite to the end the blood entered.

The time taken for the first fine thread to appear at this end (from the time of skin puncture) has been arbitrarily taken as the clotting time.

The reason that beading and clotting always begin at the end the blood entered may be that blood platelets stick to the glass wall of the tube even as the blood flows along it, and so become more numerous at the end the blood entered. The difference in clotting time between the two ends of the tube is considerable when long capillary tubes are used, but is minimal in the 3 cm.×1 mm. tubes used in this study.

Observations

1. It was quite remarkable how consecutive tests on the same patient always gave the same result. It was usual to repeat a test whenever an unexpectedly short clotting time was encountered but, assuming of course that there had been no gross error of technique, such as sweat on the finger, violent squeezing, blood allowed to run round the nail fold, bottle too hot, etc., all of which shorten the clotting time, the second result was always exactly the same as the first. This may come as a surprise to those who have condemned the test for its inconsistency.

2. It was even more remarkable how tests on consecutive patients before operation also gave, with few exceptions, the same, or nearly the same result (within a minute either way), thus demonstrating that the normal range is quite a narrow one, and at the same time establishing the normal for that particular set of capillary tubes. They were "7½-minute tubes" or "8-minute tubes" because that was the clotting time given at that time by the great majority of patients.

3. The capillary tube method used in this study has shown itself to be so reliable over so many years that one has come to have the greatest confidence in it. The secret of success no doubt is in the tubes themselves. The failure of others to produce comparable results would appear to lie less in errors of technique than in a failure to appreciate the importance of aging, and the importance of segregating completely the different batches of capillary tubes. It is the greatest mistake to assume that all capillary tubes, or for that matter all test tubes, are identical in their effect on blood coagulation. They are never identical unless they have been made and aged under identical conditions. Owing to the peculiar properties of glass, freshly drawn capillary tubes give short and somewhat erratic clotting times, but as the tubes age they behave more and more uniformly and give longer and longer clotting times until eventually they give a clotting time which is approximately twice the original figure. In other words, blood clots twice as fast in new tubes as it does in old. This fundamental observation is the key to consistent and accurate clotting time estimations.

4. Now that the reliability of the method has been established beyond question, it may be useful to summarize some of the other advantages of the test:

(*a*) The capillary tube is a convenient, self-filling expendable container which is ideal for holding a small sample of blood virtually out of contact with the air.

(*b*) The tubes have been meticulously prepared and stored; they are quite clean. Since a fresh tube has to be used for each test, there is no risk whatever that thrombin or any other substance still remains adsorbed to the glass from a previous experiment.

(*c*) No venipuncture is required. There is a real advantage here in that untrained personnel can perform the test, and it eliminates any possibility of the clotting time being affected by passage of the blood through a needle and syringe.

(*d*) The equipment is simple and easily portable. The test can quickly be done on the spot anywhere, at any time, by anyone willing to master a simple technique.

Clinical Application

Postoperative thrombosis still occurs with distressing frequency. The incidence

in adults undergoing major surgery may vary between 1% and 5%, depending on the class of patient, the nature of the operation, and the care with which it is done. For the purpose of discussion it is convenient to divide postoperative thrombosis into primary and secondary, primary thrombosis being the direct result of operation, anesthetic, etc., and secondary thrombosis, which is less common and occurs later, being related to operation but acually determined by a late complication or intercurrent infection.

Primary postoperative thrombosis usually manifests itself within two weeks of operation. Sometimes the initial thrombotic episode is entirely symptomless, and it is only later, when there is a second clot, or an extension of the first, or an embolus, that a diagnosis is made. In the belief that this first episode often occurs quite early, about the middle of the first week, a certain routine of pre- and postoperative clotting time estimations, using the equipment and technique described above, was instituted in the second half of 1948 and is still continuing.

Material.—This includes all the adult private patients submitted to major surgery by me in the last 10 years, 635 cases in all. There was no selection. Patients who had previously had a postoperative or postpartum deep vein thrombosis were accepted, including a few who had been refused operation elsewhere on that account. The operations were general surgical or gynecological.

Preoperative Clotting Times.—Clotting times were done on all patients within a few days of operation in order to sort out the few whose clotting times were short, and also to keep a continuous check on the capillary tubes in use. It is not suggested that patients who have short preoperative clotting times are all candidates for postoperative thrombosis, or that candidates for thrombosis all have short preoperative clotting times; however, it is reasonable to suppose that a clotting mechanism which is already upset or unstable may easily be further upset by operation.

Usually no reason could be given for a short preoperative clotting time, though occasionally there was a suspicion that it was connected with a recent acute infection, such as influenza, or a more chronic infection such as cholecystitis. When a short clotting time was encountered, operation was postponed until the clotting time rose to normal, which it invariably did. Most clotting times recovered fairly promptly, in a few days or a week, though occasionally a case was encountered whose clotting time remained depressed for a much longer period.

A good example of this latter type is the case of a woman, aged 45, who was to undergo hysterectomy for fibroids. Apart from the fibroids and a mild secondary anemia she appeared to be quite healthy, yet her clotting times, using 9-minute tubes, were as follows: Her first test was 6½ minutes. One might have passed this as near enough to normal if one had been using 7-minute or 7½-minute tubes, but it was not good enough for a 9-minute tube. It must be remembered, too, that hysterectomy for fibroids carries with it a special risk of postoperative thrombosis because large uterine veins are ligated not far from the internal iliacs, and there is the possibility of damage to pelvic veins by manipulation, packs, and retractors. The clotting time three days later was again 6½ minutes. One week later it was just under 5 minutes, and when repeated, just under 5 minutes. After two more weeks it was 4½ minutes, and when repeated, 4½ minutes. On the same day an independent laboratory estimated her capillary tube clotting time to be 2 minutes! Over the next four weeks her clotting times slowly improved and even rose above normal for a while before leveling off at 9 minutes. She then underwent hysterectomy without incident, and her postoperative clotting times were also 9 minutes. Nine-minute tubes were used throughout, ex-

cluding, of course, the one laboratory estimation of 2 minutes. No other patient during that whole period gave a clotting time of less than 8 minutes. One cannot escape the conclusion that a definite abnormality existed in those early weeks, and one was very grateful that the patient's condition allowed the operation to be deferred until the clotting mechanism returned to normal.

Operation was also postponed if possible, regardless of clotting times, if there had been an infection such as influenza within the preceding month.

Postoperative Clotting Times.—Postoperative clotting time estimations were planned to sort out those patients whose clotting mechanism became unstable in the early postoperative period. It was felt that if the clotting mechanism had not been upset by the middle of the first week after operation, it was unlikely to become unstable thereafter unless there were some complicating factor such as dehydration, sepsis, or an intercurrent infection. Accordingly the clotting time was done routinely on the second and again on the third postoperative day. Usually there was no deviation from the normal, and in these cases, if convalescence was straightforward, no further clotting times were done. If there was a mild fall in the clotting time on the second or third day, the test was repeated daily until the clotting time returned to normal. Also if convalescence was complicated or stormy, clotting times were sometimes continued beyond the third day as indicated. Clotting times were continued beyond the third day routinely in cases of abdominoperineal resection for cancer of the rectum, because of the large raw area and the risk of infection.

In a few patients, 1.3% of the total, the clotting time fell progressively toward danger level. The lower it fell the more frequently were clotting time estimations done. Bergquist [1] and Cummine and Lyons,[4] using different techniques, thought that the danger level was in the neighborhood of 3 minutes, but in this study 3 minutes was thought to be too low when properly aged capillary tubes were used. Instead, a clotting time that was half the normal clotting time for the tubes in use was assumed to be the danger level. Heparin was given when this level was reached, or even a little before this level if night was approaching (because of the difficulty of doing accurate clotting time determinations by artificial light), or if other features—mild cyanosis, rapid sedimentation, and heavy plasma fibrinogen B [4]—were present,

In cases that showed mild cyanosis or a leaden complexion the drop of blood on the finger was dark in color too, so dark sometimes that the patient remarked about it. No doubt this feature has often been observed in cases of established thrombosis but has been attributed to pulmonary complications.

It was noted that blood taken for a fibrinogen B test in a 13×100 mm. tube sometimes separated with great rapidity, separation being advanced within 15 or 20 minutes and so complete within the hour that the test could be run without centrifuging. The fibrinogen B test was that described by Cummine and Lyons.[4] Only a strongly positive test was thought to be significant; a weak or doubtful positive was ignored.

These features were not all present in every case (the numbers are too small for analysis), but they were observed with such frequency in the patients with short clotting times, as they have been in cases of established thrombosis, that they appear to be part of the picture. Another finding in all the patients with short clotting times was that when heparin was given there was a degree of heparin resistance or tolerance,[5] in that the response to a standard dose of heparin was less than the normal. This heparin resistance was made use of to determine the duration of heparin treatment. Heparin was continued for as long as but only as long as the state of heparin resistance lasted.

Heparin Administration.—Heparin of the strength 5,000 international units per cubic centimeter was used throughout. It was given every four hours by subcutaneous injection.[3] It was thought unwise to change to the 25,000 I.U. per cubic centimeter solution when it became available, and to an infrequent dose schedule, because one wished to avoid as far as possible peak, trough, and rebound effects with their attendant dangers. In any case it is wise to stick to a single strength of heparin, and thereby avoid any possibility of under- or overdosage through the accidental use of the wrong solution.

Injections were made deeply into the subcutaneous fat over the abdomen through a fine sharp needle. The intramuscular route was avoided on the grounds, theoretical perhaps, that a painful hematoma at the injection site, should it occur, might interfere with ambulation. Actually there is little risk of painful hematoma, or of bleeding at the site of operation, with the moderate dosage used in this study, and with the rather precise control possible with properly aged capillary tubes. The intravenous route was ruled out as being impracticable because nurses in this country are not permitted to give intravenous injections.

A usual dose was 5,000 I.U. every four hours, though the first dose might be larger if an emergency was thought to exist. Clotting times were done between three and four hours after an injection, twice daily at first and then once a day. The aim was to keep the clotting time a little above normal, at from 10 to 12 minutes. A clotting time of 15 minutes or more was an indication to reduce or omit the next dose.

Heparin was stopped when the state of heparin resistance vanished, as it did in from 2 to 10 days (average 5 days), often quite suddenly. This point was recognized by the need to reduce progressively the dose of heparin required to maintain a fixed clotting time, or by the clotting time suddenly soaring on a fixed dose of heparin.

Heparin was the only anticoagulant used in this series. Its advantages are well known, and the disadvantage of cost is partly offset by the more elaborate and expensive laboratory control required for the oral anticoagulants. Again, the shorter duration of treatment in this series, and sometimes the shorter hospital stay, should also be taken into account when comparing the costs.

Results

There has been no case or even suspicion of a case of primary postoperative thrombosis since this investigation began 10 years ago. It must therefore be concluded that any potential cases of primary postoperative thrombosis must have been in the heparin-treated group (eight cases). Heparin may have been given to one or two patients who didn't need it, but it was felt that it was better to err on the safe side when dealing with a disabling and potentially lethal disease. However, most of the heparin cases were so similar to cases of established thrombosis, except that a clot was not permitted to occur, that it was felt that a definite threat existed, and that in one or two cases the threat was a severe one. It was fascinating to watch what one believed to be the threat of thrombosis advance and recede again.

Two cases of secondary postoperative thrombosis occurred. One was a man, aged 38, operated on for a direct inguinal hernia. Four days after his discharge from hospital a late virulent wound infection developed, which was uninfluenced by antibiotics. Chest pain appeared on the 12th day of the wound infection, and calf pain and tenderness appeared two days later.

The other was a woman, aged 60, who underwent abdominoperineal resection for carcinoma of the rectum, and whose convalescence for the first five weeks was quite satisfactory. Thirty-nine days after operation she was readmitted with pseudomembranous enterocolitis. That same evening she went into severe shock in spite of massive fluid replacement. The very next day

there was clear evidence of bilateral femoral thrombosis and thrombosis of the left calf. Again on the 46th day after operation a second attack of enterocolitis was followed at once by a severe hemiplegia. At that time, April, 1950, the special risk of thrombosis in pseudomembranous enterocolitis was not appreciated; in fact the disease itself was not recognized as such until later.

These two cases illustrate what I mean by secondary postoperative thrombosis. In the first case it is fair to assume that the thrombosis occuring in the fourth week after operation was chiefly determined by the prolonged severe wound infection and would not have occurred if convalescence had been uneventful. In the second case gross fluid loss and circulatory collapse were followed immediately by thrombosis in the sixth and again in the seventh week after operation. Possibly staphylococcal infection played a part also.

In retrospect both these cases of secondary postoperative thrombosis might have been prevented by proper vigilance, but the problem isn't an easy one. It is not always possible to keep a proper check on patients after they have left the hospital, especially when they reside at some distance.

Two cases of phlebitis in preexisting internal saphenous varices occurred within the first two months after operation. It is difficult to know how to classify them, because stasis in a large varix and an unhealthy vein wall may be the determining factors.

The first patient developed a patch of superficial phlebitis a little below the knee seven weeks after operation. Since she did not report it at the time, there was no investigation or treatment.

The second case of internal saphenous phlebitis was not entirely unexpected. The patient, a woman aged 72, had traveled some distance to have a prolapse repaired; however, there were three factors which made operation at that time inadvisable. The first was that she had not felt completely well since an attack of Asian influenza followed by pneumonia and bronchitis two months previously; the second was that the clotting time was 6 minutes (7¾-minute tube) and the drop of blood on the finger was dark in color; the third was that she had a very large varicosé left internal saphenous vein. It was explained to her that operation was inadvisable at that time, and that in any case operation on the vein should take precedence over the other. However, she was a very determined woman. The varicose vein had given her no trouble, she said. She insisted that she would never return if she were sent home, and that she would soon become bed-ridden and useless. In the end, after much argument, one agreed to take a calculated risk and to operate on the prolapse. One was fairly confident that thrombosis could be prevented during her postoperative stay in hospital, but one had no idea how long it would be before her clotting mechanism returned to normal. Her postoperative clotting times while she was in hospital were all below normal but not dangerously so. She was discharged on the 11th postoperative day. Three days later she had a clot 3 in. long in the varicose left internal saphenous vein at midthigh level. She was readmitted for an emergency Trendelenburg operation. Four days later her clotting time fell to danger level, and she was given heparin for the first time; however, one was able to discontinue the heparin after two days and to discharge her four days later with a normal clotting time. Thus she had her two operations after all, but in the wrong order, and returned home a little chastened but otherwise quite well.

There were no corresponding cases of postoperative phlebitis in a deep vein previously damaged by a postoperative or postpartum thrombosis. On the other hand, there were two cases of old white leg with recurring attacks of deep vein phlebitis who were apparently cured by operation, in each case the removal of a diseased gallbladder.

They have remained well for eight and nine years respectively.

Comment

As far as it goes, this investigation confirms the observations of Bergquist, Cummine, and others that the initial postoperative thrombosis is preceded by a marked shortening of the clotting time. It is not suggested that this or any other feature of the prethrombotic state will regularly be found after thrombosis has occurred and been recognized, nor is it suggested that the same features will necessarily be present before a second clot forms or the first one enlarges. Once the initial clot has been allowed to form, the clot itself becomes a complicating factor, by its mechanical presence causing stasis, by its tendency to spread and to cause reflex phenomena, and possibly by material absorbed from it into the blood stream. In other words, thrombotic and embolic episodes predispose to recurrence. Obviously the ideal is to stop the first clot from forming, not to rescue the patient afterwards.

It is felt that some small degree of progress has been made in this direction, and one faces the future with cautious optimism. Probably the great majority of our surgical patients run no risk whatever of primary postoperative thrombosis, and therefore don't need special exercises, anticoagulants, or nursing in the head-down position. It is hoped that the capillary tube method used in this investigation will be of value to others in sorting out these patients and in assessing the risk run by the remainder. No doubt perplexities and disappointments lie ahead, and indeed are to be expected when dealing with such a versatile and treacherous disease; nevertheless, there seems to be real hope that the scourge of primary postoperative thrombosis can be materially reduced without too great an expenditure of time and trouble.

Summary

A capillary tube clotting time method which gives extremely consistent results has been described in detail.

The main features of the method are the use of a smaller capillary tube, using the "beading time" to eliminate unnecessary cutting of the tube, the complete segregation of different batches of tubes and, most important, the proper aging of the tubes before they are put to general use. Broadly speaking, blood clots twice as fast in new tubes as it does in old.

A simple routine of pre- and postoperative clotting time estimations on adult patients undergoing major surgery was instituted in the latter half of 1948 in an effort to predict and forestall primary postoperative thrombosis and embolism.

Prophylactic anticoagulant treatment was given when the postoperative clotting time fell to half or close to half the normal figure, as it did in 8 out of a total of 635 patients (1.3%).

Heparin was the only anticoagulant used. It was given in frequent small doses by the subcutaneous route. The duration of treatment, from 2 to 10 days in this series, average 5 days, was governed entirely by the duration of the patient's heparin resistance or tolerance.

There has been no case or suspicion of a case of primary postoperative thrombosis since this investigation began 10 years ago.

78 Symonds St.

REFERENCES

1. Bergquist, G.: Über postoperative Thrombosen: Vorläufige Mitteilung, Acta chir. scandinav. 83:415, 1940.

2. Brown, D.: Personal communication to the author, 1957.

3. Cosgriff, S. W.; Cross, R. J., and Habif, D. V.: The Management of Venous Thrombosis and Pulmonary Embolism, S. Clin. North America 28:324, 1948.

4. Cummine, H., and Lyons, R. N.: A Study in Intravascular Thrombosis with Some New Conceptions of the Mechanism of Coagulation, Brit. J. Surg. 35:337, 1948.

5. de Takats, G., and Fowler, E. F.: The Problem of Thrombo-Embolism, Surgery 17:153, 1945.

The Roentgen Diagnosis of Mitral Stenosis*

I. E. KIRSH, M.D., and J. F. KINNEY, M.D., Hines, Ill.

The roentgen diagnosis of mitral stenosis and its differentiation from mitral insufficiency are more important than ever now that mitral commissurotomy is available.

The ideal patient for mitral commissurotomy is one who has pure mitral stenosis, or at least no predominating insufficiency, with no involvement of any of the other heart valves, and who has pulmonary congestion but no right heart failure. Auscultation may be misleading because there may be a loud systolic murmur when the mitral valve is predominantly stenotic; surgery will benefit the patient.

Roentgen examination is often of help. Radiographs furnish more exact information than fluoroscopy and provide a permanent record besides. We have found films in the anteroposterior and lateral positions most helpful, together with the right oblique. (The left oblique view is of little value for determining left ventricular enlargement.) Fluoroscopic examination is useful in detection of calcification of the valves. We have also been able to demonstrate calcified valves on body-section radiographs (laminography).

We try to diagnose specific heart chamber enlargement. If the left atrium and right ventricle are enlarged but the left ventricle is not enlarged, this means that mitral stenosis is present. If the left ventricle is also enlarged, there is either mitral insufficiency or aortic insufficiency or both.

Submitted for publication May 1, 1959.

From Department of Radiology, Veterans Administration Hospital.

* Surgery illustrated. Shown as a Scientific Exhibit of the Section on Radiology at the 107th Annual Meeting of the American Medical Association, San Francisco, June 23-27, 1958.

Displacement of the barium-filled esophagus is the important x-ray finding. An enlarged left atrium often (but not always) displaces the esophagus to the right in the anteroposterior film. If the esophagus is pushed to the left, this is practically always because the aorta, to which it is attached, is atheromatous and swings leftward. In the right anterior oblique position, the esophagus is pushed posteriorly, well above the diaphragm in mitral stenosis. In this position, there is always convexity of the anterior cardiac border, due to right ventricular enlargement. The left lateral film is usually the most valuable one in this series. If the mitral valve is mainly stenotic, the left atrium is enlarged (displacing the esophagus posteriorly well above the diaphragm). If there is mitral insufficiency, the left atrium and left ventricle are both enlarged and the esophagus is displaced posteriorly all the way down to the diaphragm. In rare cases a "giant" left atrium may displace the esophagus in a long curve down to the diaphragm. In these cases, mitral insufficiency is usually present. In the lateral view, right ventricular enlargement makes the heart enlarge anteriorly.

Plain chest films often provide valuable information. A heavily exposed posteroanterior film may show a double density within the heart shadow, a valuable clue to the presence of enlarged left atrium. Hemosiderosis and disseminated bone nodules in the lungs can sometimes be seen in films of patients with mitral stenosis (or insufficiency). They are probably due to transudation of plasma and red blood cells into the alveoli, resulting from pulmonary vein congestion, with later organization. Hemo-

siderosis may resemble silicosis but generally shows less sharply outlined nodules. It is distinguished from passive congestion because the shadows are stable over a period of time. Photomicrographs, obtained from our autopsied cases or lung biopsy show foci of alveoli containing macrophages stuffed with hemosiderin, and in these foci, connective tissue stains show fibrosis in the alveolar walls. That the nodules are really bone and not areas of calcification will be recognized from the photomicrographs.

Transverse septal lines were brought to the attention of most of us by Peter Kerley, a British radiologist. He called them "B

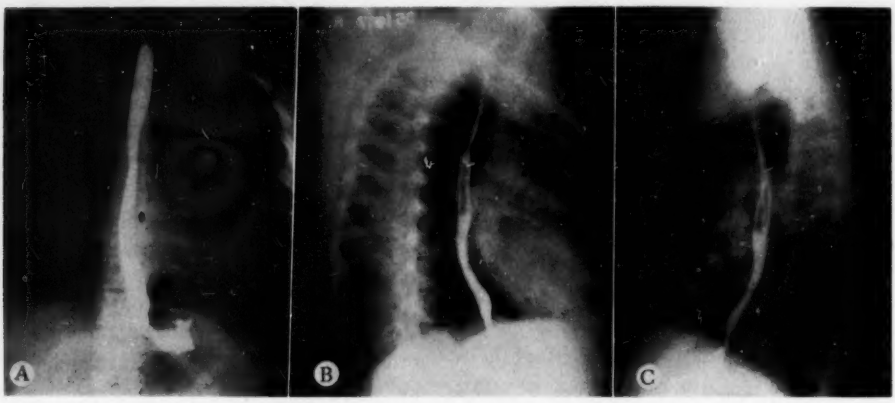
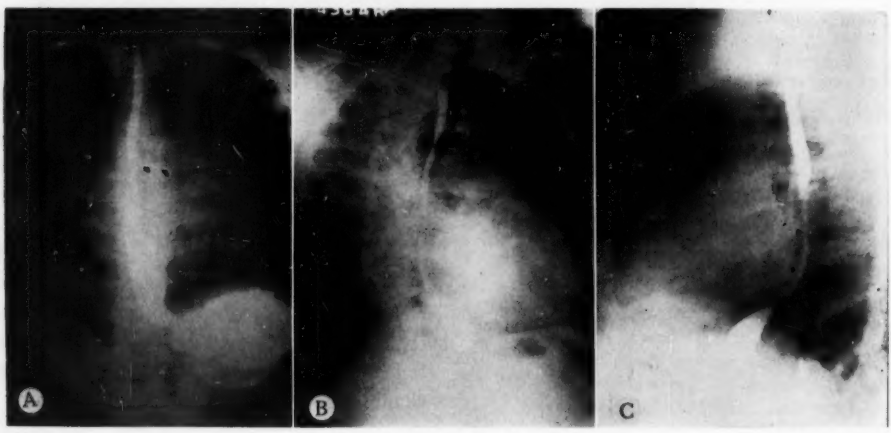


Fig. 1.—*A*, mitral stenosis. The esophagus is displaced to the right by enlarged left atrium. *B*, in the right oblique position, there is a high posterior impression on the esophagus. The right ventricle is enlarged (anterior convexity). *C*, in left lateral view, there is a high posterior impression on esophagus (left atrium). The left ventricle is not enlarged.

Fig. 2.—*A*, mitral insufficiency. The esophagus is compressed at the level of the atrium. A "double density" is seen. The left-main bronchus is elevated (arrows). *B*, in the right oblique, no clear deviation of the esophagus is seen. *C*, in the lateral position, there is compression and posterior deviation of the esophagus in a long curve, probably due to enlarged left ventricle and auricle.



lines." (The "A" and "C" lines he spoke of received less notice.) They are short (about 1 cm.), very thin, transverse lines, most frequently seen in the costophrenic angle on either side but sometimes extending upward along the axillary line. They are best shown in lightly exposed films. It is generally thought that they are caused by thickened interlobular septa, due to lymphatic vessels engorged by edema. Fleischner and Reiner showed that hemosiderin deposits in the interlobular septa could produce these lines. They frequently persist after mitral surgery. These lines have been found also in silicosis, resolving pneumonia, and lymphangitic carcinoma.

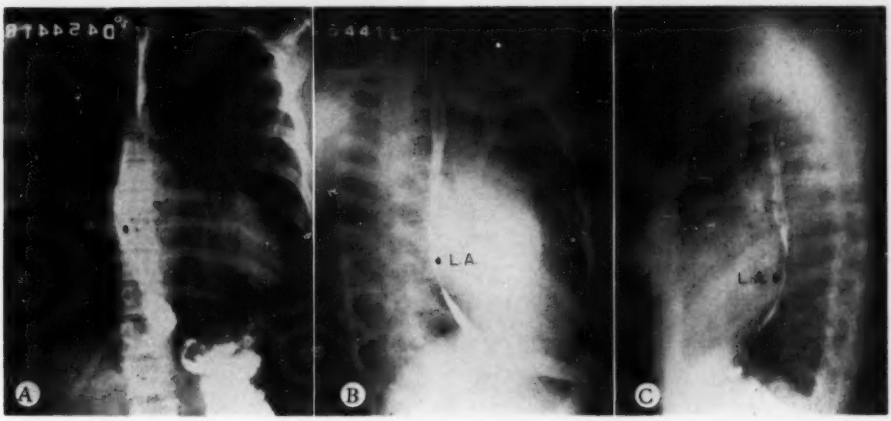
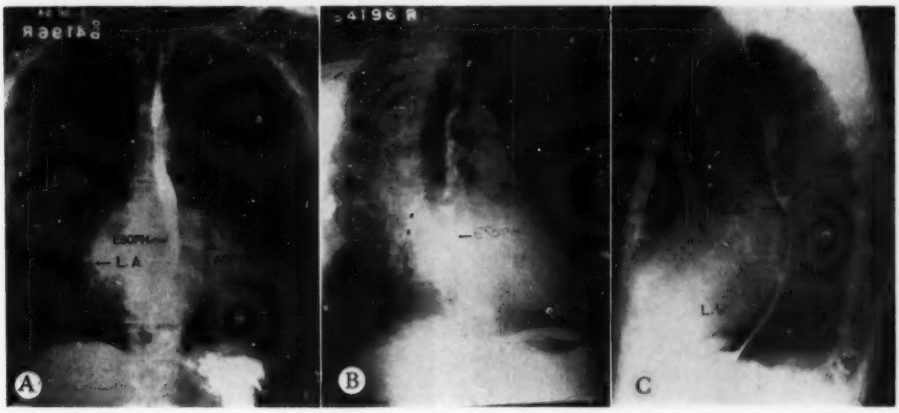


Fig. 3.—*A*, mitral stenosis. Anteroposterior film shows a "double density" and deviation of the esophagus to the right. *B*, right oblique view shows localized posterior displacement of the esophagus (enlarged left atrium). The round density to its right is the breast shadow. *C*, lateral film shows that the esophagus is displaced posteriorly in the region of the left atrium but not in the lower (ventricular) segment. Right ventricle enlarged.

Fig. 4.—*A*, mitral insufficiency. There is a "double density" due to enlarged left atrium. The esophagus is displaced to the left because of an atheromatous aorta. *B*, right oblique view is the least helpful of the three on this patient (insufficient rotation). *C*, lateral view shows posterior displacement of the esophagus over a long curve. Left ventricle is enlarged, as well as left atrium.



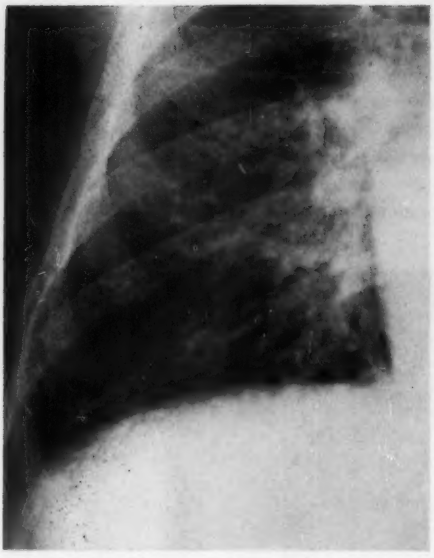


Fig. 5.—Septal lines are seen in the costophrenic angle (short, thin, transverse lines). There are some bony nodules. Hemosiderosis shown by multiple nodular deposits in lung.

Fig. 6.—In this case of mitral insufficiency, septal lines and hemosiderosis are present, as well as bone nodules.

Fig. 7.—Many bone nodules are present. Mitral stenosis.

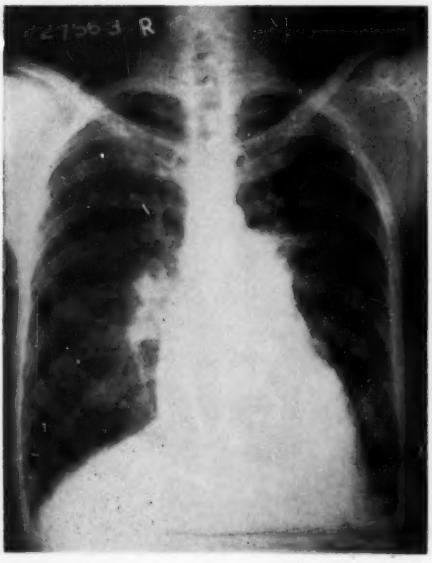


Fig. 8.—This patient with mitral stenosis has bone nodules and hemosiderosis. Congestion of the upper lobe pulmonary veins can also be seen.

Fig. 9.—Mitral insufficiency. Hemosiderosis and bone nodules. See Figure 10.

TABLE 1.—*Comparison of Mitral Stenosis and Insufficiency*

A. Mitral stenosis.	
1. Enlarged left atrium	
2. *No* significant enlargement of left ventricle	
3. Enlarged right ventricle	
B. Mitral insufficiency	
1. Enlarged left atrium	
2. Enlarged left ventricle	
3. Enlarged right ventricle	
C. May be present in either mitral stenosis or insufficiency	
1. Calcification of mitral valve	
2. Disseminated bone nodules in lungs	
3. Pulmonary hemosiderosis	
4. Septal lines at bases of lungs (Kerley)	

TABLE 2.—*Recognition of Enlarged Left Atrium*

1. Ordinary chest film (posteroanterior)
   (*a*) "Double density" within heart borders
   (*b*) Prominent pulmonary segment of left heart border
2. Anteroposterior esophagram ("Bucky")
   (*a*) "Double density" within heart borders
   (*b*) Deviation of the esophagus to the right
   (*c*) Prominent pulmonary artery segment of the left heart border
3. Right anterior oblique esophagram
   (*a*) High posterior deviation of the esophagus (left atrium)
   (*b*) Prominent pulmonary artery segment (right ventricle)
4. Left lateral esophagram
   (*a*) High posterior deviation of esophagus (left atrium)
   (*b*) No lower deviation of esophagus
   (*c*) Decreased retrosternal space (right ventricle)

TABLE 3.—*Criteria for Mitral Commissurotomy*

1. Mitral stenosis, with progressive symptoms
2. Little or no mitral insufficiency *
3. No involvement of any valve other than the mitral
4. Pulmonary congestion
5. No right ventricular failure
6. No excessive cardiac enlargement

* Open (cardiac bypass) surgery now makes available a definitive corrective procedure for patients with mitral regurgitation (Lillehei).

TABLE 4.—*Roentgen Diagnosis of Mitral Stenosis*

I. Valuable positions	
A. Anteroposterior esophagram ("Bucky")	
1. Double density within cardiac shadow	
2. High deviation of esophagus to the right	
3. Prominent pulmonary artery segment	
B. Left lateral esophagram	
1. High posterior deviation of esophagus	
2. *No lower deviation* of esophagus	
3. Decreased retrosternal space	
C. Right anterior oblique esophagram	
1. High posterior deviation of esophagus	
2. Prominent pulmonary artery segment	
II. Sometimes valuable (but mitral insufficiency not excluded)	
A. Ordinary chest film (posteroanterior)	
1. Double density within cardiac outline	
2. Disseminated bone nodules in lungs	
3. Septal lines at bases of lungs (Kerley)	
4. Pulmonary hemosiderosis	

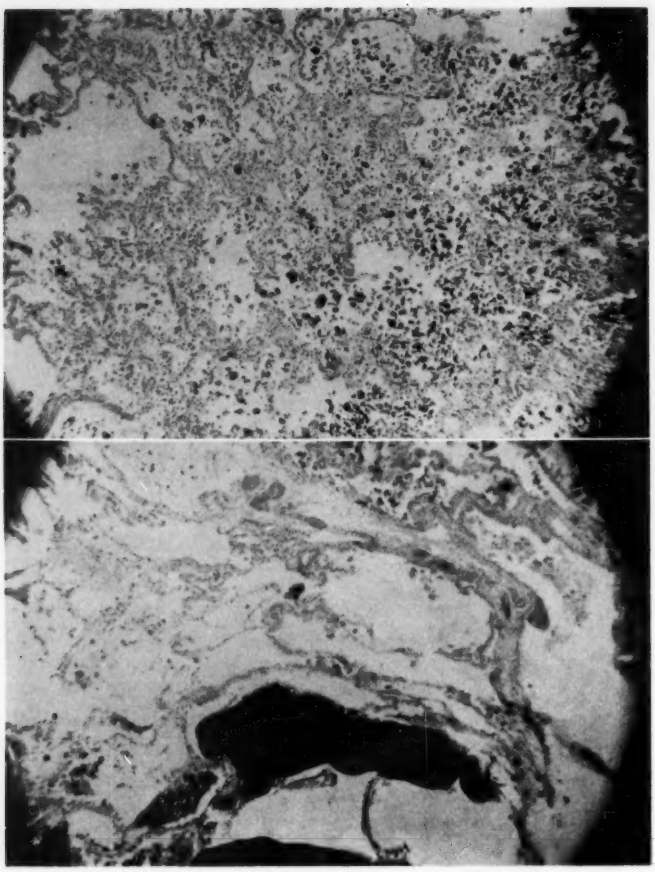


Fig. 10.—Photomicrographs on lung of patient in Figure 9 show foci of hemosiderosis, and bone nodules, with bone trabeculae.

TABLE 5.—*Relative Value of Roentgen Films and Radioscopy (Fluoroscopy)*

A. Roentgen films have these advantages
1. Earlier signs are recognizable
2. A permanent record is made
3. Less radiation to the patient (and physician)
4. The lung findings are more readily seen
B. Radioscopy has these advantages
1. Calcified mitral valve is more easily recognized
2. The patient can be readily examined in a variety of positions

BIBLIOGRAPHY

Dealy, J. B., Jr.: Mitral Valve Disease: A Radiologic Approach to a Physiological Diagnosis, New England J. Med. 254:825-829 (May 3) 1956.

Fleischner, F. G., and Reiner, L.: Linear X-Ray Shadows in Acquired Pulmonary Hemosiderosis and Congestion, New England J. Med. 250:900 (May 27) 1954.

Grishman, A., and Kane, I. J.: Disseminated Calcified and Bony Nodules in the Lungs Associated with Mitral Disease, Am. J. Roentgenol. 53:575-581 (June) 1945.

Jacobson, H. G.; Poppel, M. H.; Hanenson, I. B., and Dewing, S. B.: Left Auricular Enlargement, Am. Heart J. 43:423-437 (March) 1952.

Pendergrass, E. P.; Lame, E. L., and Ostrum, H. W.: Hemosiderosis of Lungs Due to Mitral Disease, Am. J. Roentgenol. 61:443-456 (April) 1949.

Wells, H. G., and Dunlap, C. E.: Disseminated Ossification of the Lungs, Arch. Path. 35:420-426 (March) 1943.

Zinsser, H. F.: Selection of Patients for Mitral Commissurotomy, Am. J. Med. 17:804-810 (Dec.) 1954.

Veterans Administration Hospital.

The Surgical Management of Functional Adrenal Hypercorticism

ROBERT C. OVERTON, M.D.; JOHN W. OVERSTREET, M.D., and RALPH V. FORD, M.D., Houston, Texas

The improvement of laboratory techniques for diagnosis of abnormal adrenal states has permitted the internist to present to the surgeon a greater variety of patients as possible candidates for treatment of overactivity of the adrenal cortex. The time-honored designation of "Cushing's syndrome" need not apply to this expanded group of patients since they may be considered to be in an earlier phase of "hyperadrenocorticism." Observations of a small group of these patients who have been subjected to total bilateral adrenalectomy constitute this report.

We believe that hyperadrenocorticism is initially a cyclical disease, which rarely is self-limited and most commonly is progressive. Further, if repeated observations are made on patients suspected clinically of having functional hypercorticism, the patients will persistently present these laboratory evidences (corticotropin-induced hyperresponsiveness), and the clinician is justified in recommending definitive therapy. In the absence of a chemotherapeutic agent to inhibit adrenocortical function (without prohibitive toxicity), one must consider total adrenalectomy for these patients. Willingness to subject the patient to this rather drastic procedure is proportional to the clinician's knowledge of the prognosis of untreated hypercorticism. Statistics are not fully available on this point, but there is a general clinical opinion that this disease is not totally benign.[13]

It is the purpose of this communication, therefore, to report certain aspects of the problem of functional adrenal hypercorticism in terms of diagnosis, surgical management, and follow-up of the patient.

Submitted for publication April 6, 1959.

From the Cora and Webb Mading Department of Surgery and the Departments of Medicine and Pharmacology, Baylor University College of Medicine.

Materials and Methods

The subjects of the current study were 1 male and 15 female patients with varying degrees of hypercorticism, vital statistics of whom are presented in Table 1. Medical management of these patients was unsatisfactory, and the patients were submitted to total adrenalectomy at the end of varying periods of observation (3 to 12 months).

In addition to the usual metabolic and general diagnostic studies, special studies of the adrenal steroids were conducted. Prior to and after two injections (at 12-hour intervals) of corticotropin zinc (80 units) intramuscularly, 24-hour urine collections were obtained. These urines were analyzed for 17-ketosteroid and 17-ketogenic steroid by the Norymberski technique as modified by Sobel.[11,12,17] The studies were repeated at 30- to 60-day intervals until it was determined that the patient was in an advancing or persistent state of hyperadrenocorticism. The criteria for bilateral total adrenalectomy in this initial group of patients have been (1) a more than threefold increase in the excretion of 17-ketogenic steroid following

TABLE 1.—*Preoperative Findings: Summary of Sixteen Patients*

Age, Yr.		Sex		Significant Symptomatology		
Average	Range	Male	Female	Hyperadrenocorticism	Hypertension	Masculinizing
35	18-53	1	15	9	6	1

corticotropin (ACTH) stimulation, with an absolute increase of 50 mg. per 24 hours, and (2) a persistent or advancing clinical syndrome in spite of accepted medical management.

The clinical data concerning the 16 patients have been summarized in terms of ketogenic steroid excretion, blood pressure, and weight prior to and three months after bilateral total adrenalectomy.

Surgical Management

Contraindications for surgical removal of the adrenals have been an age greater than 55 years and renal impairment manifested by a BUN greater than 30 mg. %. Congestive heart failure is not a contraindication, as 3 of the 16 patients were essentially bedridden from cardiac failure for one year or more prior to adrenalectomy.

Preoperative management has been simplified, consisting only in the usual measures employed in any major surgical procedure. This may include digitalization and diuresis in the severely edematous patient. Preoperative medication in general has consisted of the standard preparations used for all abdominal operations with avoidance of large dosages of long-acting barbiturates not only preoperatively but in induction in order to assure greater blood pressure stability. We believe that preoperative priming with exogenous steroids such as hydrocortisone is not only unnecessary but is actually contraindicated; however, previous surgical literature [1,4,6,15,16] would, in part, disagree with this approach.

The transabdominal approach for removal of the adrenal glands is selected because it permits adequate assessment of the adrenals, permits evaluation of the genitourinary organs in the female, and provides an opportunity for treatment of a variety of unrelated but coexistent abnormal intra-abdominal conditions present in some patients. An upper transverse abdominal incision not only affords access to these regions but allows one to inspect, palpate, and mobilize both adrenal glands before deciding the procedure to follow, particularly with regard to unilateral or bilateral removal. The presence of gross tumor, like the presence of histological changes, may have no correlation with physiological changes in the patient.

The right and left adrenal glands are approached laterally by division of the parietal peritoneum inferior to the hepatic and splenic flexures of the colon, respectively. Gerota's fascia is opened, and separation of the adrenal gland from the kidney is avoided so that by downward traction upon the kidney the gland can be made more accessible. Careful ligature of the left adrenal vein as it enters the left renal and of the right middle adrenal vein as it enters the vena cava is secured before division. Most of the smaller arteries and veins are much more readily managed with the application of silver clips. The ovaries are carefully inspected before adrenal ablation is carried out, and pathological changes which may be amenable to surgical treatment are corrected. For example, in those patients with large, stony-hard, fibrous, encased ovaries a wedge resection, as is recommended for the Stein-Leventhal syndrome, is performed. Associated biliary tract disease is corrected and an appendectomy performed.

As previously mentioned, no preoperative priming with supplemental steroid is instituted, but at the beginning of the procedure, through a separate intravenous infusion 100 mg. of hydrocortisone in 1,000 cc. of 5% dextrose in isotonic saline is started at a slow rate. After both adrenals have been removed, the patient usually receives approximately 30 to 40 mg. of hydrocortisone. Blood replacement varies from none in those cases in which blood loss has been minimal to a maximum of 4 units. Although blood loss is usually relatively small, it is exceedingly important that one be accurate with its replacement since a deficit at this point greatly complicates further postoperative management.

The immediate postoperative management of these patients has been greatly facilitated in our institution by the introduction of an "Intensive Care Unit" where

TABLE 2.—*Indices to Immediate Postoperative Problems Following Total Bilateral Adrenalectomy*

Indices	Primary Hydrocortisone Deficiency	Primary Na Cl Deficiency	Hypovolemia
Blood pressure	↓↓	↓	↓
Pulse rate	↑	NC	↑↑
Urine Flow	↓	↓	↓
Temperature	↑	NC	NC

the patient is placed after his removal from the recovery room. Accurate and repeated observations of vital signs and hourly urinary output provide the indices for supportive medications and immediate postoperative management (Table 2). Maintenance of normotensive blood pressure levels and an adequate urinary output are the principal goals. Vasopressor agents are not necessary and probably are contraindicated. In spite of the ablation of the adrenal medulla, these patients can and will maintain an adequate blood pressure if hydrocortisone and moderate amounts of salt are administered. The requirement for hydrocortisone postoperatively is somewhat less in this group of patients than previous studies indicate.[1,4,6,15,16] During the first 24 hours the average hydrocortisone requirement has been 200 mg. intravenously administered by constant slow infusion. Occasionally, more than 9 gm. of sodium chloride is necessary, particularly if the patient has been on a severe preoperative diuretic regimen. The volatile temperature response of these patients may afford a dramatic index to the necessity for more rapid administration of hydrocortisone. The presence of a persistent tachycardia in the immediate postoperative period is a good indication that the patient is either hypovolemic or deficient in hydrocortisone replacement. Repeated determination of the hematocrit and serum and urine electrolytes has not been of practical help in the management of these cases. In a number of the early cases the hematocrit fell strikingly for approximately 10 to 12 days postoperatively to levels of 20 cu. mm. or more, but this did not in any way correlate with the clinical status of the patient. These findings are of considerable interest, and investigations have been carried out with these changes which occur in blood volume, total body water, and extracellular fluid volume.

On the first postoperative day intravenous hydrocortisone is continued in a decreased amount (Table 3), and by the second postoperative day it is supplemented by oral hydrocortisone. With the transabdominal approach the patients have much less ileus than with the flank or retroperitoneal approach, permitting the rapid resumption of oral feedings and medication. Intramuscular hydrocortisone is not nearly so effective as oral medication and is not satisfactory under these conditions. The subsequent postoperative course is characterized by a simple rapid reduction of oral hydrocortisone to levels which are surprisingly small, averaging approximately 30 to 40 mg. in a divided dose daily. This dose is further reduced rapidly in the postoperative outpatient, particularly in patients who

TABLE 3.—*Postoperative Management of Total Bilateral Adrenalectomy*

	Hydrocortisone		Na Cl		H_2O	
Day	Mg.	Route	Gm.	Route	Liters	Route
Operative	200	I.V.	9	I.V.	3	I.V.
1	150	I.V.	9	I.V.	3	I.V.
2	100	I.V.	9	I.V.	2	I.V.
	100	Oral			1	P.O.
				Regular Diet		
3	120	P.O.	9	P.O.	2	P.O.
4	60	P.O.	9	P.O.	3	P.O.
5-10	40	P.O.	9	P.O.	3	P.O.

Fig. 1.—*A*, photograph demonstrating preoperative appearance of 40-year-old woman with fairly typical Cushing's features but whose primary indication was hypertensive cardiovascular disease with intractable congestive heart failure. *B*, postoperative photograph of same patient. The patient now has no evidence of hypertension or heart failure.

were operated upon for severe edema and hypertensive cardiovascular disease in an effort to reduce cardiac requirements rapidly to a more physiological status. Supplementary salt is usually not necessary in the diet although the patient is instructed to salt food to his taste.

In general, uncomplex surgical management has been stressed. A simple abdominal operation is employed; no preoperative measures are used to complicate the picture, and intravenous administration of hydrocortisone during the first two days is rapidly superseded by oral medication with a diet. In spite of the fact that many of these 16 patients were severe hypertensive cardiovascular problems preoperatively, there has been no mortality, and the morbidity has been minimal. Simple management of these problems has been possible with an early diagnosis, and definitive therapy has been carried out before irreversible physiological changes could occur.

Results

Pre- and postoperative photographs (Figs. 1-4) demonstrate typical examples characterizing the two broad groups of the series, namely, general hypercorticism and hypertension with associated adrenal hyperresponsiveness.

The over-all clinical improvement in these patients has been striking, both subjectively and objectively,[5] the important objective data being summarized in Table 4. While the preoperative excretion of 17-ketogenic steroid was elevated and demonstrated an abnormal increase following corticotropin (ACTH) injection, the absence of adrenal tissue following surgery is proved by the failure to respond to corticotropin. While the blood pressure in the preoperative state averaged 170/107, the postoperative blood pressure was 120/80. This has a very definite clinical implication, since most of the patients presented problems involving the cardiovascular system with heart failure. The reduction of blood pressure as well as alterations in the metabolism of salt and water following adrenalectomy has been extremely beneficial to this group of patients. Body weight preoperatively averaged 204 lb. and in the postoperative state at the end of three months averaged 171 lb. This is not to imply that bilateral total adrenalectomy is feasible

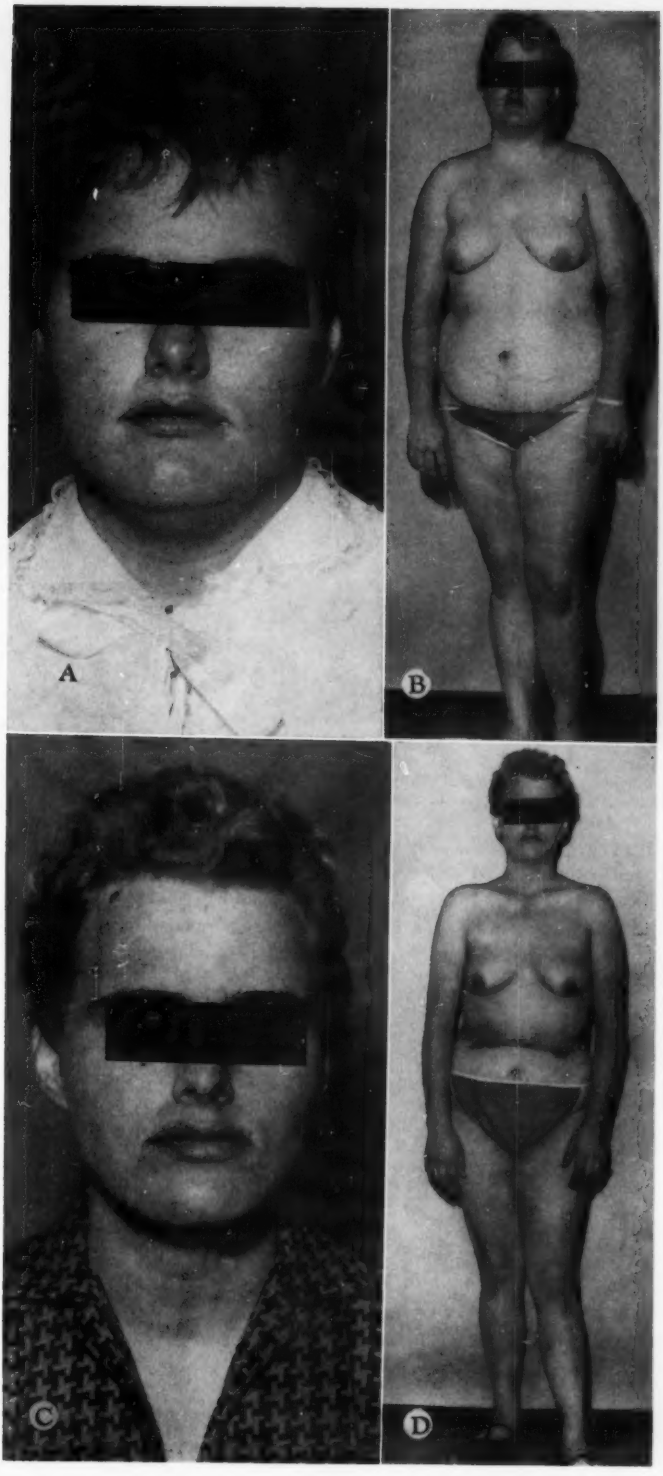


Fig. 2.—*A*, photograph of 19-year-old woman with obesity, hypertension, amenorrhea, weakness, and emotional instability. *B*, photograph demonstrating body contour and hair distribution. *C*, photograph of same patient three months' postoperatively demonstrating striking changes in facial contour. (There has been almost complete cessation of facial hair growth.) Menses are now normal. *D*, postoperative photograph demonstrating change in body contour and small transverse incision.

Fig. 3.—*A*, preoperative photograph of 45-year-old woman with only suggestive Cushing's characteristics but long-standing history of hypertensive cardiovascular disease intractable to all previous therapy, including thoracodorsal sympathectomy. *B*, postoperative photograph of same patient. She is now normotensive, with no evidence of heart failure.

therapy for obesity but merely to indicate that obesity is one of the problems of hyperadrenocorticism which can be controlled by the procedure in most instances.

The patient who was operated on primarily for masculinizing tendencies with abnormal menstrual periods and gross enlargement of the clitoris has experienced a return of the

Fig. 4.—*A*, photograph of 29-year-old woman with early Cushing's syndrome (amenorrhea, obesity, hypertension, weakness, and emotional disturbance). *B*, postoperative photograph of same patient three months later.

TABLE 4.—*Clinical Data: Averages of Sixteen Patients*

17-Ketogenic Steroid Excretion (Mg/24 Hr.)				Blood Pressure		Body Weight, Lb.	
Preoperative		3 Mo. Postoperative					
Control	After ACTH	Control	After ACTH	Preoperative	3 Mo. Postoperative	Preoperative	3 Mo. Postoperative
37	159	15	12	170/107	120/80	204	171

Normal values for 17-Ketogenic steroid excretion: Control, less than 30; after corticotropin, less than 75.

menstrual cycle to normal and a 50% reduction in size of the clitoris in less than three months. It may be of additional interest that the patient with the greatest degree of 17-ketogenic steroid (and not 17-ketosteroid) excretion following corticotropin presented the operative findings of Stein-Leventhal ovary. Nevertheless, this patient was also subjected to a total bilateral adrenalectomy. She has demonstrated a return to normal in body weight and body contour, marked decrease in hirsutism, and establishment of normal menstrual periods.

The average hospital stay for the group was nine days. At the end of three months the average dose of oral hydrocortisone required for maintenance was 7 mg. per day.

Comment

The application of surgical principles to hypercorticism or Cushing's disease is not a new one, but surgical mortality in the past prohibited the procedure in most instances. However, the availability of potent orally active adrenal steroids as supportive therapy has changed this concept, and certain patients should now be observed and considered for surgery at an earlier date. The subjects of the current study admittedly had not developed full-blown cases of Cushing's disease. The criterion for the diagnosis of functional hypercorticism is as yet not established. Although some [4] have used as a measure a threefold increase in 24-hour urinary steroid excretion, others [7-10] have been more conservative. We have used the criterion [2,7] of a minimum increase in 17-ketogenic steroid (primarily glucocorticoid) excretion of 50 mg. per 24 hours and a greater than threefold increase (over the control) following corticotropin stimulation. We believe that many of these patients presented a problem of functional hypercorticism at a very early stage in the disease but that their condition of hypercorticism was advancing and becoming more persistent or consistent. We therefore subjected them to the radical procedure of bilateral total adrenalectomy. This approach must of necessity be tentative, and these patients must be closely observed and compared with patients who do not receive benefit from this particular surgical procedure in order to establish the relative prognosis of radical surgical treatment in contrast to nonspecific medical treatment (dietary reduction, diuretics, antihypertensive therapy, and psychotherapy).

Certain clinical concepts, however, may be presented at this very early stage from observing this limited number of patients. We believe that the patients have very definitely improved in terms of their cardiovascular and hypertensive status, that they have achieved a greater degree of emotional stability, and that they have been rid of a significant catabolic factor operative in their body economy.

We further feel that the surgical management of these problems is easier than previously thought and described.[1,3,4,6,14-16] The dose of hydrocortisone as supportive therapy is smaller than previously reported, and the important factor in long-term management is to educate the patient for conditions of stress during which he must be aware of the need to increase the dose of hydrocortisone to a higher level.

The purposes of this communication are, first, to present initial data on a very radical procedure for treatment of functional hypercorticism and to emphasize the simplicity and ease of management of these patients by the procedure of total bilateral adrenalectomy; second, to emphasize the benefits that the patients derive from this approach; third, to emphasize the desirability of having a chemotherapeutic agent which will accomplish the same result as bilateral total adrenalectomy for patients who present evidence of an even earlier stage of functional hypercorticism.

Conclusions

Sixteen patients have been observed and treated for functional hypercorticism by total bilateral adrenalectomy. They have been followed for periods of 3 to 18 months and have received distinct benefit from this procedure. These patients have been treated at a stage in which their disease may be considered to be functional and not a fully developed "Cushing's syndrome." Emphasis on the ease and simplicity of this form of management is presented.

The authors are indebted to John A. Nickell Jr. for his technical assistance in preparing this manuscript.

Texas Medical Center.

REFERENCES

1. Bowers, R. F.: Bilateral Adrenalectomy for Severe Hypertension, J.A.M.A. 154:394, 1954.

2. Burnett, R.; Rukes, M.; Kolb, F., and Forsham, P. H.: Functional Diagnosis of Different States of Adrenocortical Hyperactivity, abstracted, J. Clin. Endocrinol. 14:775, 1954.

3. Ejrup, B., and Franksson, C.: Total Adrenalectomy in 5 Cases of Malignant Hypertension, Acta med. scandinav. (Supp. 312) 154:225, 1956.

4. Ellison, E. H., and Hamwi, G. J.: Adrenalectomy for Hyperfunctioning Lesions of the Adrenal Cortex, A.M.A. Arch. Surg. 76:843, 1958.

5. Ford, R. V., and Overton, R. C.: Observations on Functional Hyperadrenocorticism, to be published.

6. Harrison, J. H.; Thorn, G. W., and Crescetullo, M. G.: Study of Bilateral Total Adrenalectomy in Malignant Hypertension and Chronic Nephritis: Preliminary Report, J. Urol. 67:405, 1952.

7. Hinman, F.; Steinbach, H. L., and Forsham, P. H.: Preoperative Differentiation Between Hyperplasia and Tumor in Cushing's Syndrome, J. Urol. 77:329, 1957.

8. Laidlaw, J. C.; Reddy, W. J.; Jenkins, D.; Abu Haydar, N.; Renold, A. E., and Thorn, G. W.: Advances in the Diagnosis of Altered States of Adrenocortical Function, New England J. Med. 253:747, 1955.

9. Lindsay, A. E.; Migeon, C. J.; Nugent, C. A., and Brown, H.: The Diagnostic Value of Plasma and Urinary 17-Hydroxycorticosteroid Determination in Cushing's Syndrome, Am. J. Med. 20:15, 1956.

10. Nabarro, J. D. N.; Moxham, A., and Walker, G.: Stimulation and Suppression of the Adrenal Cortex in Cushing's Syndrome, J. Clin. Endocrinol. 18:586, 1958.

11. Norymberski, J. K., and Stubbs, R. D.: Indirect Analysis of Corticosteroids, Biochem. J. 66:176, 1956.

12. Norymberski, J. K.; Stubbs, R. D., and West, H. F.: Assessment of Adrenocortical Activity by Assay of 17-Ketogenic Steroids in Urine, Lancet 1:1276, 1953.

13. Plotz, C. M.; Knowlton, A. J., and Ragan, C.: The Natural History of Cushing's Syndrome, Am. J. Med. 13:597, 1952.

14. Schermer, J. F.; Caris, T. N.; Bowers, W. F., and Blount, P. E.: Cushing's Syndrome Treated by Bilateral Total Adrenalectomy, U.S. Armed Forces M.J. 7:272, 1956.

15. Simkin, B.: Long-Term Management of Patients After Adrenalectomy, California Med. 87:383, 1957.

16. Skanse, B.; Gydell, K.; Wulff, H. B., and Koch, F.: Cushing's Syndrome and Its Response to Adrenalectomy, Acta med. scandinav. 154:119, 1956.

17. Sobel, C.; Golub, O. J.; Henry, R. J.; Jacobs, S. L., and Basu, G. K.: Study of Norymberski Methods for Determination of 17-Ketogenic Steroids (17-Hydroxycorticosteroids) in Urine, J. Clin. Endocrinol. 18:208, 1958.

Compound Dislocation of the Knee with Popliteal Artery Injury

JOHN G. RAFFENSPERGER, M.D., and JOSEPH HINKAMP, M.D., Chicago

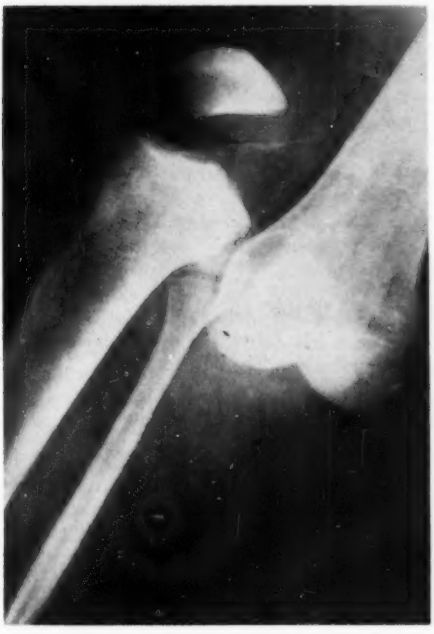
Compound dislocation of the knee associated with laceration of the popliteal artery is an unusual injury and one which frequently results in amputation or disability due to arterial insufficiency. We are fortunate in having treated such a case with a successful outcome and we feel that the management of this patient is worth reviewing since success in such a case seems dependent on attention to each detail.

Our patient was a 28-year-old man, who entered Cook County Hospital four hours after a tractor trailer had run over his right knee. He was in severe pain and mild shock; blood loss from his wound was not remarkable. Examination of the leg revealed the lateral condyle of the femur to be protruding through the skin below the knee, and the leg below this was cold, pulseless, and anesthetic. An x-ray (Figure) revealed a posterolateral dislocation of the femur on the tibia.

Submitted for publication April 19, 1959.

Department of General Surgery of the Cook County Hospital.

Compound dislocation of the knee.



Spinal anesthesia was chosen to reduce vasospasm and to provide for muscle relaxation to facilitate reduction of the dislocation.

The wound edges were debrided, and the original wound was extended transversely across the popliteal fossa and distally down the calf. There was no bleeding during the initial incision and only minimal oozing of dark blood as generous amounts of hemorrhagic muscle were cut away. The peroneal nerve was stretched around the femoral condyle and was carefully protected. After careful wound cleansing the dislocation was reduced by flexion and traction. As the reduction was accomplished brisk arterial bleeding occurred, and it was found that the popliteal artery had been contused and completely severed. The ends of the artery were grasped with forceps and the vessel mobilized so that the ends lay together without tension even after resection of 1 cm. of contused vessel. Anastomosis was achieved with interrupted everting sutures of 00000 silk. The joint capsule, lateral ligaments, cruciate ligaments, and synovial membranes were extensively torn, but no attempt was made to suture these tissues. The wound was irrigated with saline and loosely sutured with steel wire.

While he was still on the operating table pulsations were noted in the dorsalis pedis and posterior tibial arteries. He was given papaverine, paravertebral blocks, and large doses of antibiotics for five days. The knee was held in 90 degree flexion by an anterior mold for three weeks, then gradually extended to 120 degrees, where it was held by a long leg cast for seven more weeks. Upon removal of the cast it was noted that he had a drop foot, which was thought to be on the basis of the severe stretching of the peroneal nerve by the injury. He was then given intensive quadriceps exercises and allowed to use a drop foot brace.

One year after the injury he was presented at a Cook County Hospital surgical conference. Ex-

amination then revealed equal dorsalis pedis and posterior tibial pulsations in each foot and a stable knee joint with a completely normal range of motion. There remained hypesthesia along the lateral aspect of the foot, but he was able to dorsiflex the foot without difficulty.

Comment

The sturdy arrangement of the fibrous capsule of the knee joint with the medial, lateral, and cruciate ligaments accounts for the infrequency of dislocations of this joint except on severe direct violence applied to the head of the tibia.[1] The capsule and all the ligaments save the medial collateral were completely disrupted in this case. Despite the fact that none of them were sutured, stability of the knee resulted from prolonged immobilization and quadriceps exercises.

The popliteal artery is relatively fixed at the upper end of the popliteal space by the tendinous arch of the adductor magnus muscle and distally by the soleus and gastrocnemius arches. This fixation, together with its direct contact with the posterior part of the knee joint, explains its liability to injury in dislocation of the joint.[2]

We have surveyed the literature for cases of popliteal artery injury occurring in association with dislocation of the knee. Two reviews of popliteal artery injury in the early German literature reported on eight cases; all of these ended in gangrene of the extremity and amputation.[3,4] Another case reported by Anderson resulted in gangrene and amputation.[5] Goldman succeeded in salvaging a leg even though the artery was ligated at the time of reduction.[6] Semisch reported on the only other case in which the artery was repaired by direct anastomosis.[7]

In this type of case of injury to the popliteal artery there is associated soft tissue damage in the entire area which would serve to disrupt the collateral circulation. This would tend to make the amputation rate higher than in ordinary direct arterial injury. Modern techniques in vascular surgery can be applied with success in this type of case and is the only way in which circulation to the lower limb can be maintained. The ancillary procedures used in this case, such as spinal anesthesia and paravertebral blocks, perhaps contributed to maintaining the patency of the vessel. The relative youth of this patient and the promptness of surgical intervention appeared to be responsible for the excellent result obtained.

REFERENCES

1. Watson-Jones, R.: Fractures and Joint Injuries, Ed. 2, Baltimore, The Williams & Wilkins Company, 1955.

2. Latimer Callander, C. L.: Surgical Anatomy, Ed. 2, Philadelphia, W. B. Saunders Company, 1948.

3. Brunner, C.: Zur subcutanen Verletzung der Arteria poplitea, Deutsche Ztschr. Chir. 25:99, 1886-1887.

4. Schulz, K.: Die Totalen Rupturen der Arteria Poplitea, Deutsche Ztschr. Chir. 46:476, 1897.

5. Anderson, R. L.: Dislocation of the Knee with Rupture of the Popliteal Artery and Vein, Virginia M. Month. 58:120, 1931.

6. Goldman, H.: Complete Dislocation of the Knee with Rupture of the Popliteal Vessels: Report of a Case, J. Internat. Coll. Surgeons 19:237, 1953.

7. Semisch, W.: Subluxation des Kniegelenkes nach hinten mit Zerreissung der Arteria Puplitea, Deutsche Ztschr. Chir. 243:621, 1934.

Further Considerations in the Use of Hypothermia and Intermittent Cerebral Ischemia

An Experimental Study in Primates

R. W. PORTER, M.D., Ph.D., Long Beach, Calif., and LIEUT. COL. G. J. HAYES (MC), U.S. Army

Although occlusion of the cerebral arterial circulation has been of considerable value in temporarily controlling hemorrhage during the surgical treatment of intracranial vascular anomalies, its elective use for any prolonged length of time to facilitate the removal of otherwise inoperable lesions has been limited by the substantial risk of impairing neural function. Total cessation of the circulation under hypothermia has been pioneered by the cardiovascular surgeon to allow direct attack upon lesions of the heart and great vessels. The relatively short length of time which the central nervous system will withstand total ischemia even under hypothermic conditions, however, has restricted its usefulness and has stimulated the study of means to shunt the circulation around the diseased area in order to maintain the cerebral blood supply during surgery. As such techniques are of little value to the neurosurgeon, it is important to understand the conditions for deriving the maximum possible benefit from afferent circulatory occlusion with the least risk of brain damage. The present investigation was undertaken to delineate more specifically the limits of tolerance of the organism to these procedures on an experimental level, so that they might be used clinically to the best possible advantage. Concurrently, some of the physiologic events attendant with their use were explored in the hope of finding the causes of the all too frequently observed untoward effects.

Submitted for publication April 29, 1959.

Walter Reed Army Medical Center, Washington, D.C.

Because of its advanced level of behavior, the monkey was the experimental animal used for most of these studies. Selected experiments were repeated in the chimpanzee, however, not only because of its still higher degree of intelligence, but also because under hypothermic conditions its cardiovascular system responds in a manner similar to that of the human whereas that of the monkey does not. Initial experiments were concerned with the study of the effect of prolonged hypothermia upon neural function in an attempt to confirm and amplify preexisting observations in the monkey [3,5,10] and to extend them if possible to the chimpanzee. Subsequent experiments focused upon isolating some of the critical factors involved in the successful use of induced cerebral ischemia.

Methods

These experiments were carried out on 41 monkeys (Macaca mulatta) and 9 chimpanzees. Animals were anesthetized with pentobarbital sodium (25 mg/kg.) and were intubated. Hypothermia was induced in monkeys by immersing them in a cold water bath (14 C) and in chimpanzees by packing them in ice (4 C) for a period of 60 to 90 minutes. Complete occlusion of the afferent cerebral circulation was accomplished by placing Potts' arterial clamps on the truncus communis and left subclavian arteries in the monkey, and on the innominate, left common carotid, and subclavian arteries in the chimpanzee. This was done through a left intercostal incision, which was sutured at the termination of the experiment. At the close of the experiment, animals were rewarmed in a 40 C water bath.

Various physiologic and chemical measurements were made throughout the course of the experiments. The femoral vessels were isolated and cannulated to facilitate blood pressure determina-

tions. The arterial cannula was advanced through the femoral artery into the distal portion of the aorta. The venous catheter was passed by way of the vena cava into either of the innominate veins. The cerebrospinal fluid pressure was measured in early experiments through an 18-gauge spinal needle placed in the cisterna magna. In later experiments this measurement was made through an indwelling catheter placed in the lateral ventricle prior to the experiment. All pressure measurements were made through Stathan pressure transducers and recorded simultaneously on a Sanborn polygraph. The body temperature was followed with a mercury thermometer placed high in the rectum. Electrocardiographic tracings were made through standard limb leads. Six silver electrodes were placed beneath the scalp in the frontal, parietal, and temporal regions, bilaterally, so that the electrical activity of the cerebral hemispheres could be followed throughout the course of the experiments on a six-channel Grass electroencephalograph. Artificial respiration was given with a Palmer mechanical respirator (10 to 15 cm. H_2O) when required and when the chest was open for the application of clamps. In a few experiments it was used throughout even though not required in order to evaluate its effect upon venous pressure. The blood pH was determined at frequent intervals to be certain that it remained above 7.4. The cerebral blood flow (nitrous oxide method) and the arterial-venous oxygen differences were determined in the first few chimpanzee experiments until it was established that their values did not vary significantly from those in the monkey under similar conditions. A battery of additional determinations was made, but since they did not pertain directly, they will be reported separately.

A gross evaluation of neurological function was made before the experiments and daily thereafter. Animals were observed under cage conditions and were examined while restrained in chairs.[6] A gross estimate of sensory function was obtained by observing the response to painful stimuli. Motor deficits were detected by observing the gait and the widthdrawal response to pain. The tendon and pupillary light reflexes were elicited and compared with their counterparts on the opposite side. After recovery seemed apparent, monkeys were returned to the community cage, and their ability to survive in this environment was noted.

Behavioral conditioning experiments were performed to evaluate intellectual impairment in several monkeys which had been subjected to prolonged hypothermia alone or with cerebral ischemia and yet showed no gross evidence of neurologic damage or electroencephalographic abnormality. These were designed to measure the animal's ability to perceive and discriminate previously learned stimuli and to make an appropriate motor response to them. Animals were tested on a 45-minute program which was divided into three sections.[7] During the first 15-minute period (labeled *I* on Figs. 4 and 5) a red light was presented to the animal, which indicated that unless it pressed a lever at least once every 20 seconds it would receive an unpleasant electric shock. The second 15-minute section was a rest period (*II*; indicated by a white light) during which responses were recorded, but they accomplished nothing. During the last period (*III*; green signal light) a food reward (sugar pellet) was given for every 100 responses. Approximately eight weeks were required to train monkeys to perform these behavior schedules well. At this point the hypothermia experiment was performed, and the psychological testing procedures were repeated. By comparing the performance before and after the acute experiment, the animal's ability to retain learned discriminative behavior could easily be measured. The pattern of responses during the avoidance and reward schedule and the number of needless responses during the rest period were especially significant.

The brains of all monkeys were subjected to postmortem examination. Those monkeys which did not die after the experiments were killed three to four months later. Chimpanzees surviving the experiment were not killed but were used for other unrelated experiments, and their brains are being examined as they become available.

Results

Hypothermia Alone.—Eleven monkeys and two chimpanzees were subjected to prolonged hypothermia so that the effect of this procedure alone upon the nervous system might be evaluated. Two animals each were cooled for 12, 24, and 36 hours,

TABLE 1.—*Effect of Prolonged Hypothermia on Neural Function*

No. of Animals	Temperature, C	Length of Hypothermia, Hr.	Result
1 Monkey	25-27	12	Normal
1 Monkey	28-30	12	Normal
1 Monkey	25-27	24	Normal
1 Monkey	28-30	24	Normal
1 Monkey	25-27	36	Normal
1 Monkey	28-30	36	Normal
1 Chimpanzee			
3 Monkeys	25-27	48	Severe neurol. deficit
2 Monkeys	28-30	48	1 normal; 1 with neurol. deficit
1 Chimpanzee			Normal

and five monkeys were kept hypothermic for 48 hours (Table 1). In the shorter experiments (12 to 36 hours), one animal of each pair was cooled to between 25 C and 27 C so that the integrity of the visceral reflexes was lost and artificial respiration had to be used. Three of the five animals cooled for 48 hours were treated in a similar manner. The body temperature of the remaining animals was kept between 28 C and 30 C to keep respiration spontaneous. All animals cooled up to 36 hours recovered promptly and displayed no evidence of neurologic or psychologic disturbance. Hence, in these experiments the body temperature or integrity of the visceral reflexes seemed to make little difference in the final outcome, although animals requiring artificial respiration consistently showed a higher venous and intracranial pressures.

Four of the five monkeys used in the 48-hour hypothermia experiments showed overt signs of neurologic damage following the experiment. This was manifest by hemiplegias in three, and by prolonged unconsciousness in the fourth. The fifth animal, which was one of those not requiring artificial respiration, was normal after the procedure.

Two chimpanzees were subjected to prolonged hypothermia, one for 36 hours and the other for 48 hours. Their temperatures were kept between 28 C and 30 C, and spontaneous respirations were maintained at all times. Both animals recovered, although the second required 48 hours for the complete return to consciousness.

Induced Cerebral Ischemia.—Single Period: Initial studies were concerned with determining the longest duration of a single period of total occlusion of the arterial circulation to the brain which could be maintained with a minimum risk of inducing cerebral damage. Four of seven animals subjected to such total occlusion for 15-minute periods, each at a temperature of 27 C to 29 C, died within 24 hours after the experiment. The three remaining animals

TABLE 2.—*Effect of Hypothermia and Intermittent Cerebral Ischemia in Monkeys*

No. of Monkeys	Temp., C	Minutes Arterial Occlusion										Vis. Reflex Activity	Result
		Occl.	Off	Occl.	Off	Occl.	Off	Occl.	Off	Occl.	Total Occl.		
2	28-30	10	10	10	10	10	10				40	Present	Died
2	28-30	10	10	10	10	10					30	Present	1 Normal; 1 died
4	28-30	10	30	10	30	10	20	10			40	Present	3 Normal; 1 died
2	28-30	10	10	10	20	10	30	10	40	10	60	Present	1 Normal; 1 died
8	28-30	10	10	10	20	10	30	10	40	10	80	Present	7 Normal; 1 neurologic deficit
4	28-30	10	10	10	20	10	30	10	40	10	80	Present	1 Normal; 2 died; 1 neurol. deficit
4	28-31	10	10	10	20	10	30	10	40	10	80	Present	1 Normal; 2 died; 1 neurol. deficit
4	25-27	10	10	10	20	10					20	Absent	Died
4	25-27	10	10	10							20	Absent	1 Neurol. deficit; 1 abnormal EEG; 2 intell. impairment only
4	25-27	10									10	Absent	3 Normal; 1 intell. impairment only

TABLE 3.—*Effect of Hypothermia and Intermittent Cerebral Ischemia in Chimpanzee*

Chimp.	Temp. C	Min. Total Occlusion	Vis. Reflex Activity	Result
HC-A	28	50	Present	Normal
HC-B	27	50	Present	Slow return to consciousness
HC-C	29	50	Present	Abn. EEG for 1 wk.
HC-D	28	50	Present	Normal
HC-E	26	20	Absent	Died
HC-F	27	20	Absent	Normal
HC-G	27	20	Absent	Persistently Abn. EEG
HC-H	26	10	Absent	Coma for 8 days, then gradual return to normal

recovered promptly and appeared normal. Five monkeys were totally occluded for a single 10-minute period and they recovered without incident. In view of these findings and those previously reported by others [10] all subsequent experiments involving occlusion of the afferent cerebral circulation were restricted to 10-minute periods.

Intermittent Ten-Minute Periods: Eighteen animals were used to study the number of times a 10-minute period of occlusion could be repeated at a given time and also the length of time required between periods of occlusion for recovery to take place. The schedules employed in this study and the results from their use are summarized in Tables 2 and 3. Two monkeys were subjected to total arterial occlusion for a total of 40 minutes with 10 minutes between the periods of occlusion. Both of these animals succumbed before a normal temperature was regained. The next two monkeys were subjected to only three 10-minute periods of occlusion with 10 minutes between each two periods. In these experiments one animal recovered and the other died immediately after the rewarming period. The interval between occlusion periods was increased to 20 minutes in four experiments. Three of these four animals successfully withstood a total of 40 minutes of arterial occlusion while the fourth animal died immediately after the experiment. It was suggested in the studies that with each successive period of occlusion a longer interval was required for recovery to take place. This was indicated by the time required for the return of spontaneous electrical activity in the electroencephalogram after removal of the arterial clamps. After the first 10-minute period of occlusion, electrical activity reappeared within 15 to 45 seconds. After each successive period of occlusion an additional two to five minutes was required for the reestablishment of the preocclusion electrical pattern. In view of these findings, the interval between successful periods of occlusion was gradually increased. Doing so by increments of 10 minutes each proved to be adequate.

Using this schedule, eight monkeys and four chimpanzees were subjected to a total of 50 minutes of total occlusion of the afferent circulation to the brain. All animals with the exception of one monkey seemed to stand the procedure well and showed no untoward after-effects. The eighth monkey remained in coma for three days and on awakening showed evidence of generalized cerebral deterioration. The body temperature of these animals was kept between 27 C and 29 C, and respirations were spontaneous at all times. An additional two animals were occluded for 60 minutes, but one of these animals died.

Degree of Hypothermia Required: The maximum temperature range which would protect against such an occlusion schedule was studied in four monkeys. The temperature of these animals was maintained between 29 C and 31 C, and they were subjected to a total of 50 minutes of complete cerebral ischemia. Three of these animals failed to regain consciousness and died one to four days after the experiments. The fourth animal had no apparent neurologic deficit. Temperatures in the 25 to 27 C range did not in themselves appear to be harmful in these experimental animals. At this level of hypothermia, however, the integrity of the visceral reflexes was frequently lost and this appeared to have dele-

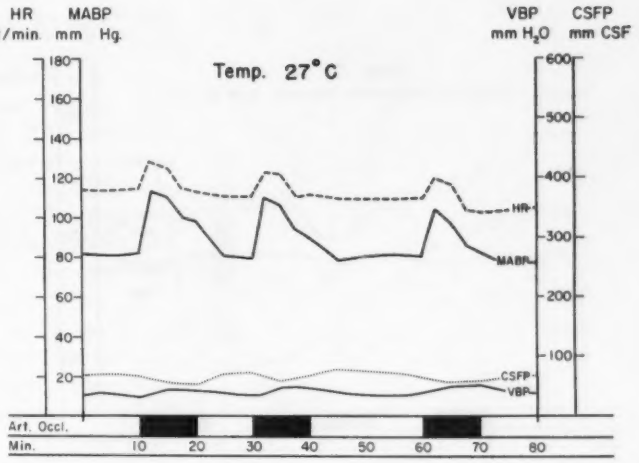


Fig. 1A.—Graph showing effects of intermittent total occlusion of cephalic arterial circulation upon heart rate (*HR*), mean arterial blood pressure (*MABP*), venous blood pressure (*VBP*) and cerebrospinal fluid pressure (*CSFP*) in a chimpanzee. Respirations were still spontaneous at this level of anesthesia and hypothermia. This and subsequent graphs were made from points taken at 2.5 minute intervals from the continuous recordings. This graph is continued in Figure 1B.

terious effects. In addition, the lower temperatures were frequently accompanied by the same type of cardiac irregularities in the chimpanzee as in the human. The monkey did not appear to be subject to this complication.

Advantage of Intact Visceral Reflexes: The effect of impairing the integrity of visceral reflexes was observed in an additional 12 monkeys and 4 chimpanzees. This was manifest by a loss of spontaneous respiration and the failure to obtain a carotid sinus response to arterial occlusion. In the previously mentioned experiments where higher temperatures were used and there was no impairment in spontaneous respiration, repeated periods of occlusion were accompanied by a gradually decreasing magnitude of the pressor response. The effect upon the blood pressure, heart rate, venous pressure, and cerebrospinal fluid pressure for each period of occlusion under such conditions is shown in Figures 1A and 1B. The blood pressure and heart rate responses were maximal within a few seconds after occlusion and then gradually returned to the baseline level. With each subsequent period of occlusion the magni-

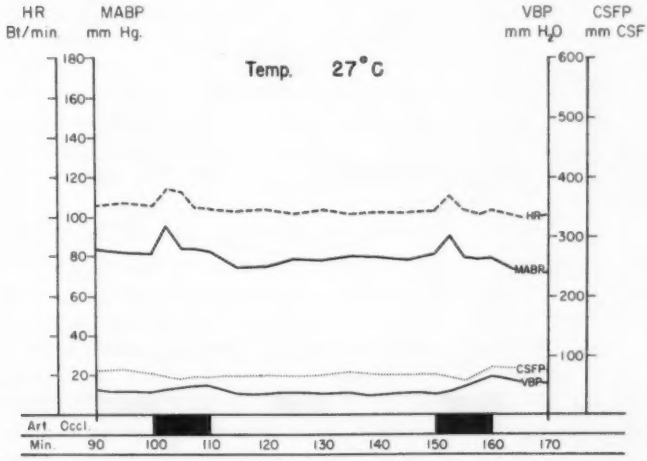


Fig. 1B.—This graph is a continuation of Figure 1A. Total occlusion time in this experiment was 50 minutes. An increasing length of time was required after each period of occlusion to insure survival of the animal. Note the decreasing magnitude of the pressor response with each period of occlusion.

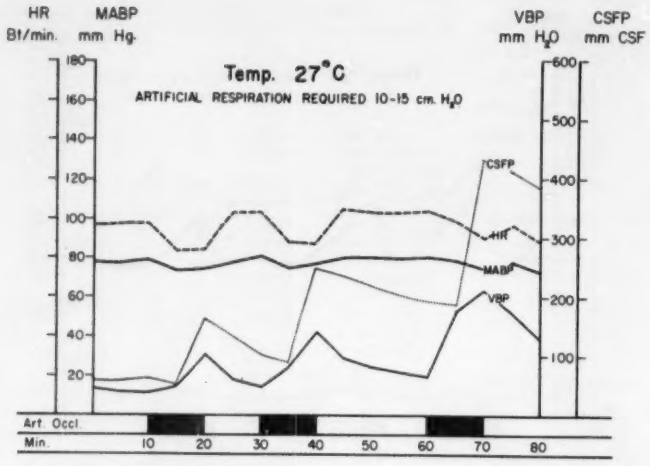


Fig. 2.—Graph showing effects of intermittent cerebral ischemia upon the same physiologic functions as in Figures 1A and 1B. In this experiment visceral reflex activity was lost at this level of anesthesia and hypothermia, so artificial respiration was required. Note increasing venous and cerebrospinal fluid pressures with each period of occlusion and loss of pressor response.

tude of the response gradually decreased and the time required for the return to the baseline level became shorter. As a rule, under the conditions of these experiments, the sixth period of cerebral ischemia was not accompanied by such a response. An immediate fall in the cerebrospinal fluid pressure during each period of arterial occlusion was short-lived and the pressure returned to essentially the preocclusion level within two minutes (not shown in Figures). When colder temperatures were employed, or when the level of anesthesia was sufficiently deep to impair spontaneous respiration, a pressor response to arterial occlusion was no longer obtained (Fig. 3). The response to three periods of occlusion under such conditions is shown in Figure 2. The increasing venous blood pressure and cerebrospinal fluid pressure with each period of occlusion is readily apparent. Four monkeys were subjected to this regimen and all four died one to three days after the experiment. An additional four animals were subjected to a similar schedule but for a total of only 20 minutes of arterial occlusion. One of these animals had definite neurologic findings consisting of a

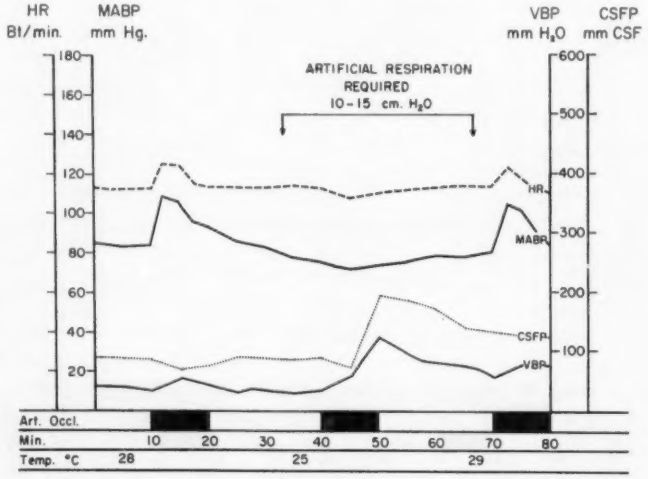


Fig. 3.—Graph showing effect of intermittent cerebral ischemia upon various physiologic functions at different levels of hypothermia in the same chimpanzee. Loss of spontaneous respiration and pressor response to arterial occlusion occurred at 26 C and returned when the temperature came up to 28 C.

hemiparesis and persistent lethargy. One of the remaining three animals had a grossly abnormal electroencephalogram as manifest by dyssynchronous slow waves (2 to 5 cps) of both hemispheres. The remaining two animals, although appearing normal and having a normal electroencephalographic tracing, showed evidence of impairment of higher neural function as evidenced by the psychological testing measures described below.

The next group of four animals was subjected to cerebral ischemia for only one 10-minute period at a temperature level where artificial respiration was required. All these animals appeared to recover and showed no gross evidence of neurologic impairment. One of these animals, however, showed definite impairment for retention of learned behavior. Four chimpanzees were subjected to arterial occlusion under these same conditions, three for a total of 20 minutes each, and the other for only 10 minutes. One animal of the first group died one day after the experiment without having regained consciousness. The second had a persistently abnormal electroencephalogram and the third appeared normal. The one chimpanzee occluded for only one 10-minute period remained unconscious for eight days, then gradually returned to normal.

The ability of animals to retain learned discriminative behavior after hypothermia and cerebral ischemia was tested in a few selected monkeys. Only those animals were tested which showed no evidence of neurologic or electroencephalographic abnormality and in which such abnormalities might be expected to be found if the experiments had been prolonged.

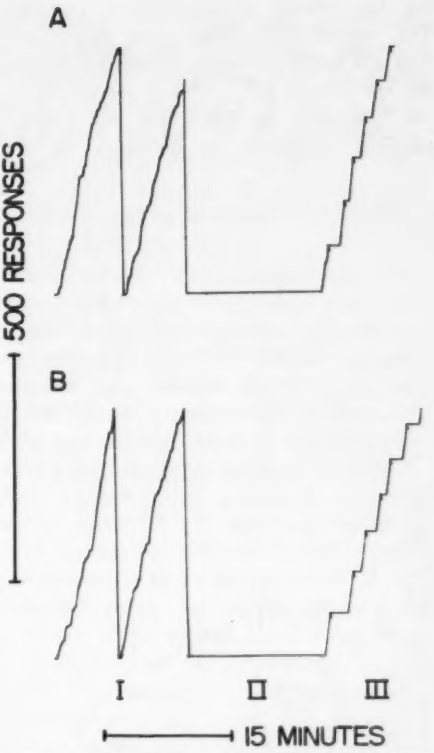


Fig. 4.—Cumulative work record which shows results of psychological testing procedures used before (*A*) and one day after (*B*) a hypothermia experiment. In this and subsequent graphs the number of responses made by the monkey is plotted against time. In the first part of the curve (*I*) the animal is responding to prevent an electric shock and does so quite effectively. In (*II*) lever presses accomplish nothing, and in neither record are any useless responses made. In the last part of the graph (*III*) each 100 responses are followed with a food reward (indicated on graph by a small downward deflection of the pen). During the hypothermia experiment the temperature was lowered to 27 C and the cephalic circulation arrested intermittently for 50 minutes on a schedule similar to that illustrated in Figures 1A and 1B with the visceral reflexes intact. There is no detectable difference in performance between *A* and *B*.

Figure 4 shows the preexperimental (*A*) and the postexperimental (*B*) records of a monkey subjected to a total of 50 minutes of cerebral ischemia under hypothermic conditions which allowed the visceral reflexes to remain intact. The intervals between periods of occlusion were increased by increments of 10 minutes each. In these graphic records the motor responses of the animal are plotted on the vertical axis against time on the horizontal one. In the first section (*I*) of the control tracing (*A*) the animal began to respond immediately after the stimulus light came on (indicating that unless he responded, electric shocks would be delivered) instead of waiting for

the first shock to begin lever pressing. The animal's responses were steady and they efficiently prevented all shocks. During the rest period, (*II*), when a second stimulus light came on, there was not a single needless response, as indicated by the straight line. The motor responses for food reward during the third section of the multiple program (*III*) were well organized without fault. The postexperimental tracing (*B*) was made the day following the hypothermia experiments and did not differ in any respect from the preexperimental tracings.

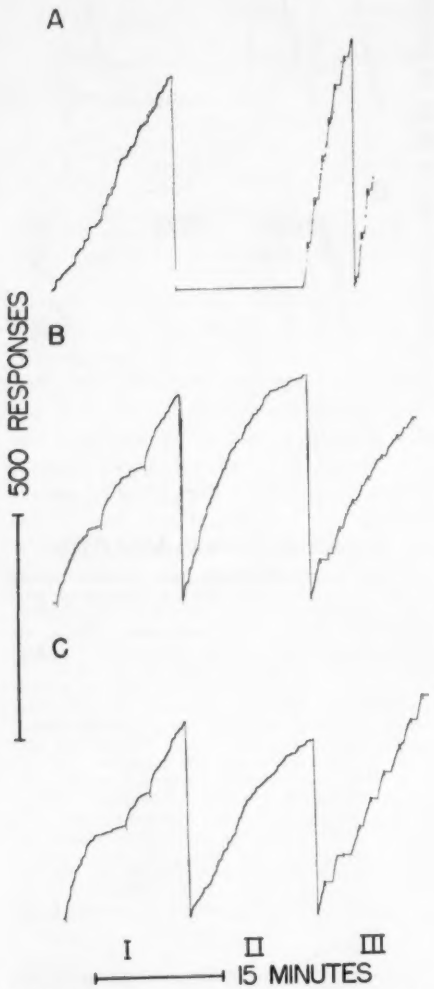


Fig. 5.—Records of psychological testing before (*A*) and after (*B, C*) a hypothermia experiment involving intermittent cerebral ischemia for only 20 minutes at 27 C, but the integrity of the visceral reflexes was lost. The animal appeared normal, but definite impairment in ability to retain learned discriminative behavior (*B*) and failure to relearn (*C*) are noted. This is indicated by failure to avoid shocks in *I*, useless responses in *II*, and disorganized pattern of responses in *III*.

Figure 5 shows the preexperimental (*A*) and two postexperimental (*B* and *C*) tracings of a monkey subjected to only two periods of cerebral ischemia under hypothermic conditions which abolished the visceral reflexes. Although the animal appeared neurologically normal and the electroencephalograms showed no abnormalities, a marked difference between the preoperative and the postoperative tracings is readily apparent. The control is similar to those of Figure 4 in that it shows no mistakes. Record *B* was made two days after the hypothermia-cerebral ischemia experiment and shows several features which indicate a loss of the ability to retain learned discriminative behavior. During the avoidance schedule (*I*) the animal did not begin responding to the red light stimulus but waited until the first shock was delivered before beginning to respond. An additional two shocks were received during the 15-minute period. During the second part of the schedule (*II*) the white stimulus light was no longer recognized as a rest period, for the animal continued to respond despite the fact that its lever presses were without effect. Even responses for food reward during the third portion of the schedule (*III*) were disorganized as compared to the control tracings. Record *C* was made four weeks after the acute experiment and indicates the same degree of impairment despite attempted retraining.

Pathologic Findings.—Examinations of the brains of animals which died during the immediate postexperimental period revealed marked venous congestion and cerebral edema. In many cases subpial petechial hemorrhages were scattered over the surface of the cerebral hemispheres. Those

surviving for more than a week showed a loss of neural elements in varying amounts throughout the cortex and basal ganglia. No specific pathologic changes were noted in those monkeys which had displayed deficits only in the intellectual sphere.

Gross and microscopic observation of the brachiocephalic arteries in no case showed evidence of thrombosis at the site of occlusion.

Comment

The results of these experiments serve to emphasize the multiplicity of factors which must be taken into consideration for the successful use of hypothermia and induced cerebral ischemia. Previous studies have shown that as the temperature is lowered the cerebral oxygen consumption is reduced,[1,2,11] enabling the brain to withstand total cessation of its afferent blood supply for substantially longer periods than it could at normal temperature. It has become increasingly clear, however, from this and other studies that arterial occlusion for single periods longer than 10 to 12 minutes is accompanied by a great risk of severe neurologic complication. Hypothermia (26 to 30 C) itself would seem to have little deleterious effect upon the function of the central nervous system, at least in periods up to 48 hours. Although animals subjected to longer periods of hypothermia showed neurologic deficit, these results are hard to evaluate, as difficulties in maintaining nutrition, and fluid and electrolyte balance complicated such prolonged studies.

The degree of hypothermia, however, is important from the standpoint of the complications which it may induce. Cardiac irregularities are known to occur in humans and in dogs and limit the lower range of useful hypothermia. A similar incidence of cardiac irritability was observed in the chimpanzee at temperatures of 27 C and below, whereas such complications were seldom seen in the monkey even at much lower temperatures.

Occlusion of the carotid and vertebral arteries has been used clinically in various combinations with encouraging results in the treatment of intracranial vascular lesions.[4,8] All four vessels have been occluded for a single period of over 14 minutes without apparent ill effects. Ischemia has been used intermittently up to a total of 47 minutes, although this particular case was complicated by vertebral artery thrombosis.[8]

Experimentally, many investigations have arrested the circulation at some point for varying lengths of time under different degrees of hypothermia.[3,10,12] McMurrey and associates have studied the effect of the afferent cerebral circulation in monkeys for single periods from 12 to 25 minutes and found a high incidence of neural damage.[10] They concluded that prolonged ischemia did not seem feasible and suggested the use of intermittent occlusion. In the present experiments a temperature of 30 C or below had to be reached to afford protection for 10 minutes of cerebral ischemia. As the lower limit of hypothermia is delineated by secondary complications, a rather narrow temperature range is available for maximum arterial occlusion. In the experimental animal under barbiturate anesthesia this was found to range between 27 and 30 C.

Thus additional cerebral ischemia could be obtained only through intermittent arterial occlusion. The problem then was essentially one of determining the frequency at which such periods could be repeated without additive effect. In early experiments, however, it became quite clear that with each succeeding period of occlusion a longer period was required for recovery. This was first suggested by the length of time required for the return of electrocortical activity after occlusion but was later proved by the neurologic end-result. If additional periods of cerebral ischemia were imposed at rapid intervals with inadequate recovery periods brain damage occurred. It was found that the minimum time which was necessary for recovery between periods of occlusion in these an-

imals had to be increased each time by an increment of 10 minutes. Should such a regimen also be necessary in the human, as would seem likely, the practical usefulness of intermittent cerebral ischemia for any substantial length of time would be markedly limited.

The status of visceral reflex activity at the time of occlusion seemed to be of considerable importance in determining the outcome of the present experiments. Important indications of this were the presence or absence of spontaneous respiration and the degree of pressor response to arterial occlusion. With the use of barbiturate anesthesia, spontaneous respiration ceased around 27 C. This is in keeping with the observations of others in dogs [2] and with those of Fay and Smith [6] who studied reflex activity in humans under hypothermia. The underlying pathophysiologic mechanism leading to neural impairment when arterial occlusion was carried out during the period of impaired visceral reflexes is not readily apparent. One contributing factor may have been related to the increased venous pressure which was observed during the period of occlusion. Presumably, this contributed to the increased intracranial pressure and in the presence of hypoxia to the ensuing neural damage. It seems unlikely that the artificial respiration per se was a responsible factor leading to neural damage. This possibility was explored in a few experiments by using mechanical respiration during the entire period of hypothermia even though it was not required, and, although the venous pressure was elevated slightly throughout the experiment, the final outcome was not altered.

The importance of psychological as well as neurological screening procedures in detecting impairment of neural function induced by hypothermia and cerebral ischemia is demonstrated by the results of the present studies. The behavioral conditioning techniques employed have indicated deficits in memory and relearning which would otherwise have gone unnoticed and thus provide a more sensitive index for the experimental evaluation of the tolerance of the brain to hypoxia.

Summary and Conclusion

An experimental analysis of hypothermia and induced cerebral ischemia was undertaken in monkeys and chimpanzees in an effort to delineate the optimal conditions for producing a bloodless operative field for the surgical approach to intracranial vascular lesions. Using barbiturate anesthesia, the range of hypothermia which would adequately protect for a 10-minute period of total cessation of the afferent cerebral circulation was found to be 27 to 30 C. Additional periods of arterial occlusion could be carried out, provided the recovery time was increased each time by an increment of 10 minutes. Intact visceral reflex activity appeared to be an important factor in minimizing the risk of neurologic deficit. From an experimental standpoint it would seem that the elective use of total intermittent cerebral ischemia for prolonged lengths of time would be limited by the recovery time required between periods of arterial occlusion.

The authors wish to express their appreciation to Dr. Joseph Brady for his advice and supervision of psychological testing procedures.

5901 E. 7th St. (4) (Dr. Porter).

REFERENCES

1. Bering, E. A.; Taren, J. A.; McMurrey, J. D., and Bernhard, W. F.: Studies on Hypothermia in Monkeys: II, Surg. Gynec. & Obst. 102:134, 1956.

2. Bigelow, W. G.; Lindsay, W. K.; Harrison, R. C.; Gordon, R. A., and Greenwood, W. F.: Oxygen Transport and Utilization in Dogs at Low Body Temperatures, Am. J. Physiol. 160:125, 1950.

3. Bigelow, W. G., and McBirnie, J. E.: Further Experiences with Hypothermia for Intracardiac Surgery in Monkeys and Groundhogs, Ann. Surg. 137:361, 1953.

4. Botterell, E. H.; Lougheed, W. M.; Scott, J. W., and Vandewater, S. L.: Hypothermia and

Interruption of Carotid, or Carotid and Vertebral Circulation, in the Surgical Management of Intracranial Aneurysms, J. Neurosurg. 13:1, 1956.

5. Callaghan, J. C.; McQueen, D. A.; Scott, J. W., and Bigelow, W. G.: Cerebral Effects of Experimental Hypothermia, A.M.A. Arch. Surg. 68:208, 1954.

6. Fay, T., and Smith, G. W.: Observations on Reflex Responses During Prolonged Periods of Human Refrigeration, Arch. Neurol. & Psychiat. 45:215, 1941.

7. Ferster, C. B., and Skinner, B. F.: Schedules of Reinforcement, New York, 1957, Appleton-Century-Crofts, Inc.

8. Lougheed, W. M.; Sweet, W. H.; White, J. C., and Brewster, W. R.: The Use of Hypothermia in Surgical Treatment of Cerebral Vascular Lesions, J. Neurosurg. 12:240, 1955.

9. Mason, J. W.: A Restraining Chair for the Experimental Study of Primates, J. Appl. Physiol. 12:130, 1958.

10. McMurrey, J. D.; Bernhard, W. F.; Taren, J. A., and Bering, E. A.: Studies on Hypothermia in Monkeys: I., Surg. Gynec. & Obst. 102:75, 1956.

11. Rosomoff, H. L., and Holaday, D. A.: Cerebral Blood Flow and Cerebral Oxygen Consumption During Hypothermia, Am. J. Physiol. 179:85, 1954.

12. Swan, H.; Zeavin, I.; Holmes, J. H., and Montgomery, J.: Cessation of Circulation in General Hypothermia, Ann. Surg. 138:360, 1953.

The Effect of Thio-TEPA on Wound Healing

HANS RATH, M.D., and IRVING F. ENQUIST, M.D., Brooklyn

It has been shown by several investigators that tumor cell emboli are present in the blood stream of patients with carcinoma. Cancer cells were demonstrated in the venous blood draining organs involved by cancer by McGrew et al.[1] and by Fisher and Turnbull.[2] Engel[3] and Moore et al.[4] have also demonstrated the presence of tumor cell emboli in the peripheral blood of patients with carcinoma. The administration of cancericidal chemotherapeutic agents at the time of surgical removal of carcinoma to destroy any tumor cells existing as emboli was suggested by Cruz, McDonald, and Cole.[5] Mechlorethamine (nitrogen mustard) and Thio-TEPA (triethylenethiophosphoramide) have been shown by Cole and his group[6] to be markedly effective in reducing the incidence of tumor cell "take" when given to animals having Walker 256 carcinosarcoma cell suspensions injected into the portal vein. The clinical use of cancericidal agents at the time of surgery for cancer has been reported by the same group of investigators,[7] and, based on this work, further clinical investigation of these agents used in this manner is currently in progress.[8]

Since the cancericidal chemotherapeutic agents are known to affect rapidly growing tissues primarily, it is important to consider the possibility that the cellular proliferation in a healing surgical wound might be affected. A diminution in the tensile strength or a delay in the gain of tensile strength of a surgical wound in a subject receiving these drugs has been considered a possibility by several workers. Krementz et al.[9] have shown a decreased tensile strength of healing sutured gastrotomy wounds in guinea pigs treated with triethylenemelamine. Farhat et al.[10] found a decreased tensile strength in laparotomy wounds in rats treated with mechlorethamine. Conn et al.[11] on the other hand, showed no interference with the healing of gastrotomy wounds in dogs treated with mechlorethamine and Thio-TEPA.

The diversity of these findings suggests the need for further evaluation of the problem. This experiment, in progress as the above findings were reported, was devised to test the effect of Thio-TEPA on the gain in tensile strength of laparotomy wounds in rats.

Method

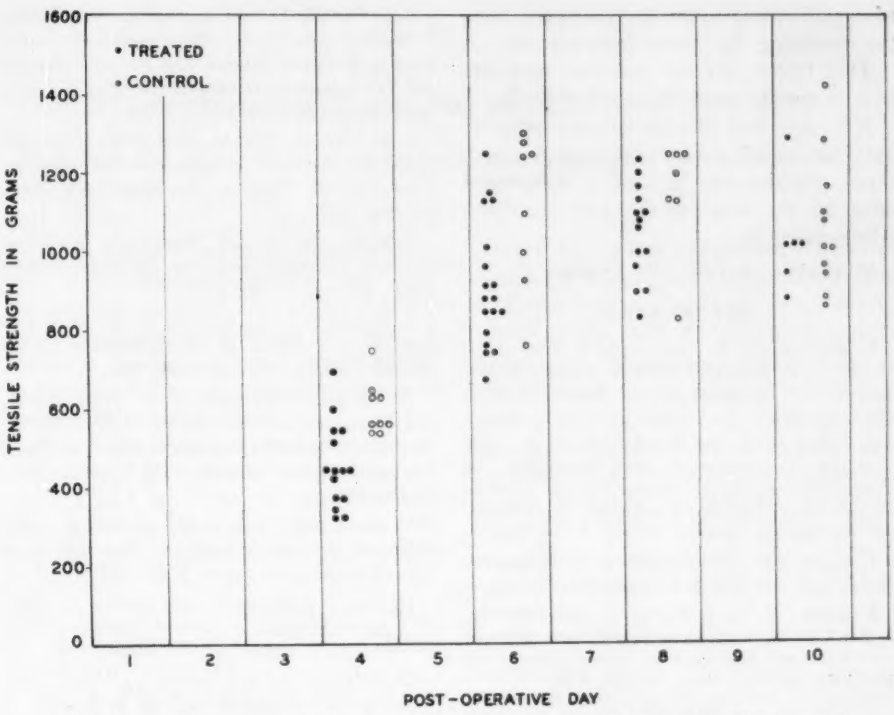
Wistar rats weighing 140-200 gm. were employed. The abdomen of the animals was shaved on the day prior to operation. The animals were anesthetized with ether and fastened to an operating board. The skin was washed with iodine tincture, and sterile technique was employed. A paramedian laparotomy incision 4 cm. in length was made. Then the peritoneum, posterior rectus sheath, rectus muscle, and the anterior sheath were closed as one layer with interrupted sutures of 0000 silk placed at 5 mm. intervals. The skin was closed with a continuous suture of 0000 silk. In animals receiving the agent, 0.4 mg/kg. Thio-TEPA was injected intraperitoneally just prior to skin closure, and 0.4 mg/kg. was injected intravenously into the tail vein on the day after operation. (This is the dosage at which Thio-TEPA is employed clinically.) Animals showing any evidence of wound infection or wound separation were excluded from evaluation.

Wound tensile strength measurements were done in 88 animals. Of these, 35 received the drug and 53 served as controls.

Animals of the control and the treated groups were killed and weighed on the 4th, 6th, 8th, and 10th days after laparotomy. The skin was dissected from the abdominal wall. Strips, 1 cm. wide, each with two silk sutures, were cut from the healing laparotomy wound. Each strip was then

Submitted for publication April 23, 1959.

Department of Surgery, State University of New York Downstate Medical Center.



Gain in tensile strength of laparotomy wounds in rats treated with Thio-TEPA, and in normal, control rats.

grasped between two clamps. A container was attached to the lower clamp, and water was slowly poured into the container. The total weight of the container necessary to disrupt the suture line was measured. Three strips from each animal were tested, and the average of these was recorded.

Results

The tensile strengths of laparotomy wounds in the treated rats and the untreated controls on the 4th, 6th, 8th, and 10th postoperative days are shown in the accompanying graph. One notes that the tensile strengths in the treated animals do not differ significantly from those of the controls, on all testing days.

Comment

The explanation for the lack of effect of Thio-TEPA on the gain in tensile strength of healing wounds may be that this drug is no longer effective at the time the gain in tensile strength normally occurs. It has been shown by Fast, Nelson, and Dennis [12] and by Nelson and Dennis [13] that when sutures are left in the abdominal wall during wound strength measurements, as in this experiment, the gain in wound strength occurs after the fourth postoperative day. Additionally, it is well known from histologic studies that fibroblastic proliferation does not begin until approximately the fourth day after operation. It is possible, therefore, that any deleterious effect on wound healing by Thio-TEPA is prevented by giving the drug prior to the onset of fibroplasia.

Summary and Conclusions

Laparotomy wound tensile strength measurements were made in 88 rats. Thirty-five were treated with Thio-TEPA on the day

of operation and on the day after operation; the remaining fifty-three were controls.

Thio-TEPA did not interfere with the gain in tensile strength of the wounds.

It is suggested that the administration of the Thio-TEPA prior to the stage of fibroplasia explains the lack of a detrimental effect of the drug on the gain in wound tensile strength.

450 Clarkson Ave. (3) (Dr. Enquist).

REFERENCES

1. McGrew, E. A.; Laws, J. F., and Cole, W. H.: Free Malignant Cells in Relation to Recurrence of Carcinoma of the Colon, J.A.M.A. 154:1251, 1954.

2. Fisher, D. R., and Turnbull, R. B., Jr.: The Cytologic Demonstration and Significance of Tumor Cells in the Mesenteric Venous Blood in Patients with Colorectal Carcinoma, Surg., Gynec. & Obst. 100:102, 1955.

3. Engel, H. C.: Cancer Cells in the Circulating Blood, Acta chir. scandinav. Supp. 201, 1955.

4. Moore, G. E.; Sandberg, A., and Schubarg, J. R.: Clinical and Experimental Observations of the Occurrence and Fate of Tumor Cells in the Blood Stream, Ann. Surg. 146:580, 1957.

5. Cruz, E. P.; McDonald, G. O., and Cole, W. H.: Prophylactic Treatment of Cancer, Surgery 40:291, 1956.

6. McDonald, G. O.; Livingston, C.; Boyles, C. F., and Cole, W. H.: The Prophylactic Treatment of Malignant Disease with Nitrogen Mustard and Triethylenethiophosphoramdide (Thio-TEPA), Ann. Surg. 145:5, 1957.

7. Morales, F.; Bell, M.; McDonald, G. O., and Cole, W. H.: The Prophylactic Treatment of Cancer at the Time of Operation, Ann. Surg. 146:588, 1957.

8. Moore, G. E., and Kondo, T.: Study of Adjuvant Cancer Chemotherapy by Model Experiments, Surgery 44:199, 1958.

9. Krementz, E. T.; Giddens, W. R., and Chapman, W. L.: Effects of Triethylenemelamine on Wound Healing, S. Forum 8:83, 1957.

10. Farhat, S. M.; Amer, N. S.; Weeks, D. S., and Musselman, M. M.: Effect of Mechlorethamine Hydrochloride (Nitrogen Mustard) on Healing of Abdominal Wounds, A.M.A. Arch. Surg. 76:749, 1958.

11. Conn, J. H.; Leb, S. M., and Hardy, J. D.: Effect of Nitrogen Mustard and Thio-TEPA on Wound Healing, S. Forum 8:80, 1957.

12. Fast, J.; Nelson, C., and Dennis, C.: Rate of Gain in Strength in Sutured Abdominal Wall Wounds, Surg., Gynec. & Obst. 84:685, 1947.

13. Nelson, C. A., and Dennis, C.: Wound Healing: Technical Factors in the Gain of Strength in Sutured Abdominal Wall Wounds in Rabbits, Surg., Gynec. & Obst. 93:461, 1951.

The Hyperglycemic Reaction of Alarm in Surgery

CARL O. RICE, M.D., Ph.D.; J. H. STRICKLER, M.D., M.S., Minneapolis, and MARTIN BECKMAN, Ph.D., New Haven, Conn.

Hyperglycemia is usually considered to be a manifestation of diabetes, and, when the routine preoperative laboratory determinations indicate no evidence of sugar in the urine, the surgeon is not usually atuned to the possibility of hyperglycemia as a postoperative complication.

Selye [1] has indicated that any type of trauma will produce an initial hyperglycemia. This, he states, is especially pronounced in traumatic injuries to the intestine or in intraperitoneal procedures. Hemorrhage, burns, x-ray irradiation, anoxia, muscular exercise, and nervous or emotional stress, all, may produce a typical hyperglycemic response.

He has also observed that there may be a secondary hypoglycemia, particularly if there has been some fasting, starving, or malnutrition preceding the systemic stress.

It is known that diet and the state of nutrition of the patient preceding the systemic stress may greatly alter the carbohydrate metabolism response, for, when the glycogen stores are depleted, the secondary hypoglycemia develops more rapidly.

That the liver is the major source of the hyperglycemia during stress is suggested by the finding of a greater concentration of glucose in the hepatic vein of the shocked dog than was found in the portal vein.

The adrenals, no doubt, play a factor in this response, for it has been observed that the administration of corticotropin (ACTH) can produce hyperglycemia or, conversely, that the hyperglycemia can be, on the whole, eliminated after adrenalectomy.

Submitted for publication Feb. 11, 1959.

Dr. Beckman, Assistant Professor, Cowles Foundation, Yale University, performed the statistical analysis.

Selye has further stated that it is often possible to detect the hyperglycemic curve of the adaptation syndrome, even in the face of giving a shocking dose of insulin.

Our clinical experience would seem to lend credence to this observation, for, in treating patients who have developed this hyperglycemic reaction of alarm, it has been our observation that a greater quantity of insulin is required to suppress the hyperglycemia of alarm than is ordinarily required for a correspondingly elevated blood sugar associated with a known diabetic.

Method of Study

A group of 24 patients were studied. A gastric or colon resection was performed on each of them. It was considered that these abdominal and intraperitoneal procedures were essentially equal in their surgical trauma and likewise that they were sufficiently traumatizing to produce some reaction of alarm.

Another group of patients upon whom less extensive surgery was performed were studied as controls.

On the morning after admission into the hospital a fasting set of blood samples were drawn. These patients were then placed on continuous parenteral feeding through an inlying intravenous polyethylene tube.[2] An intravenous solution * containing fructose was given slowly (approximately 1 liter in 8 hours), uniformly, and around the clock, beginning 24 to 36 hours before operation. The intravenous feeding was then continued uninterruptedly throughout the surgical operation and throughout the postoperative period through the third postoperative day. The rate of administration was not changed. No other nutrition was given.

Serial blood studies as indicated in the illustration were done on admission, immediately before

* 1,000 calories per liter; protein hydrolysate 80 gm.; fructose 120 gm.; ethanol 35 gm.; sodium 48 mEq.; potassium 24 mEq.; calcium 8 mEq.; magnesium 3.2 mEq.; chloride 35.2 mEq.; phosphate 48 mEq.

TABLE 1.—*Blood Studies in Cases of Gastric-Colon Resection During Continuous Intravenous Feeding*

	Fasting Admission	Intravenous Feeding Being Given: Immediate Preop.	Immediate Postop.	First Day Postop.	Third Day Postop.
Blood sugar	100.00	(76) 114	(125.4) 250	(88) 157	160
CO_2	27.58	(28.95) 25.49	(26.61) 24.06	(26.61) 24.77	27.49
Cl	107.2	(107.5) 110.33	(106.6) 105.5	(103.38) 102.3	105.6
Na	149.2	(149.9) 150.5	(148.15) 143.4	(148.7) 144.5	147.2
K	4.63	(4.79) 4.75	(4.46) 4.36	(4.52) 4.54	4.40
BUN	17.27	(17.05) 17.07	(16.05) 19.12	(18.65) 22.4	29.62
B.S.P.	6.2		18.47 --	(16.25) 35.9	--
Bl. protein	6.7	(7.06) 6.9	(7.03) 6.6	(6.97) 6.5	6.1
Albumin	3.6	(3.90) 3.6	(3.79) 3.6	(4.10) 3.5	3.1
Globulin	3.1	(3.16) 3.3	(3.86) 3.0	(2.86) 3.0	3.0
Hematocrit	40.1	(46.10) 43.3	(43.60) 44.8	(45.90) 45.8	39.6

These figures represent the mean; the figures in parentheses represent the control series.

surgery, immediately after surgery (approximately 3½ hours after the preoperative determination), 24 hours after surgery, and 72 hours after surgery.

The figures shown in Table 1 represent the mean of the determinations on 24 patients. The figures in parentheses represent corresponding observations in the control group.

In the control group of 20 patients the studies were discontinued on the first postoperative day, as it was evident that only an insignificant hyperglycemic reaction had developed and that there was no change in the electrolyte pattern.

Observations

Blood Sugar.—The preoperative blood sugar was not appreciably different from the admission blood sugar, despite the continuously running intravenous solution.

In the immediate postoperative period there was a definite rise in the blood sugar in 21 out of 22 cases for which observations were available. A binomial test on the direction of change shows that this increase is highly significant, statistically. The probability of these observations resulting from chance is less than 0.0005%. In 17 instances this rise in the blood sugar exceeded, on the average, 200 mg. %. When a marked elevation of the blood sugar was evident, it seemed to be associated with a less favorable clinical condition of the patient.

In those instances in which the immediate postoperative blood sugar rise was more extensively elevated (greater than 200 mg. %), it was observed that the 24-hour, the 48-hour, and the 72-hour blood sugar remained elevated. In some instances it had not returned to the preoperative level by the third postoperative day.

Electrolytes.—As indicated by the CO_2 determination, there was no associated disturbance in the acid-base balance as pertains to the hyperglycemia, as is frequently found with a diabetic hyperglycemia.

There was likewise no parallel disturbance in the serum sodium, potassium, or chloride levels with the hyperglycemia, although a previous study has indicated that a hyper-

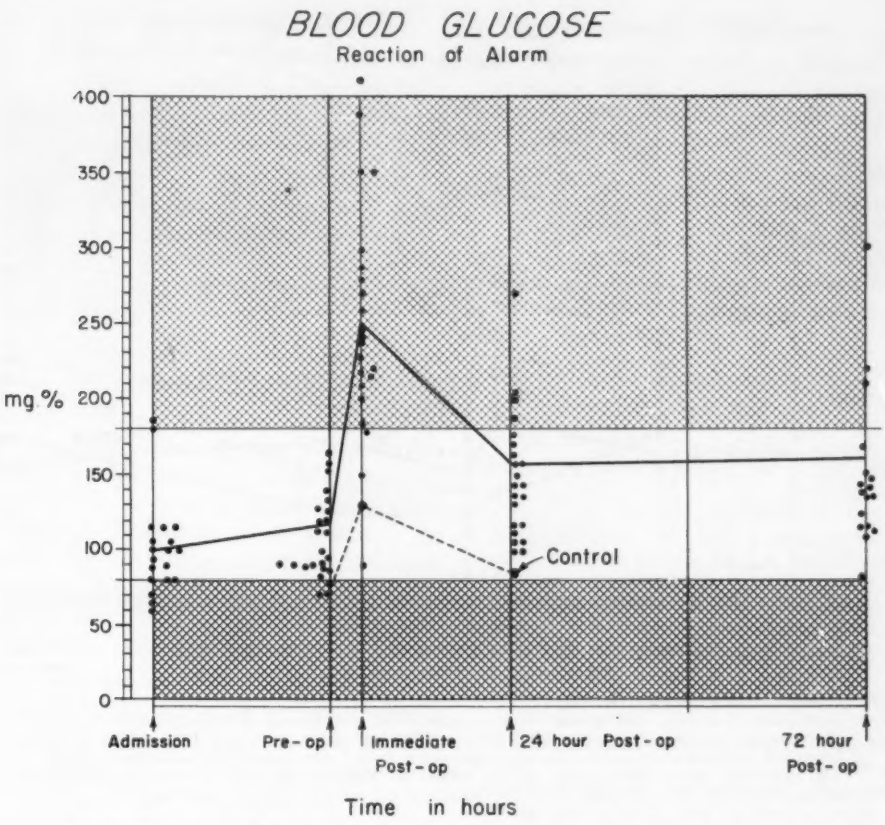


Fig. 1.—Blood sugar during the alarm of surgery. The individual determinations are indicated by the dots. The admission determinations were done on the fasting blood. The other determinations were done while the patient was receiving the intravenous feeding. The immediate postoperative rise in the blood sugar was found to be statistically significant. The control group is indicated by the broken line. Individual determinations for the control group have not been included on the graph.

glycemia was a frequent association with an electrolyte imbalance.[3,4] There was a consistent drop in all of the electrolytes in the immediate postoperative period. The fall in the sodium level was statistically significant at the 1% level whereas the decline in the chloride and CO_2 was at only the 5% level of significance. No statistically significant relationship was found in the case of potassium, blood urea nitrogen, or hematocrit value, where the changes were minor, although they appeared to be consistently altered in the immediate postoperative period.

Sulfobromophthalein Determinations.—When the blood sugar was found to be elevated about 200 mg. %, a sulfobromophthalein (Bromsulphalein; B.P.S.) determination was done on the following day. Associated with the rise in the blood sugar there was a rise in the B.P.S. in every instance, as indicated in Table 2.

This finding suggests a source for the temporarily disturbed carbohydrate metabolism in the liver.

On the basis of observations on another small group of patients showing this reaction, we believe that these hyperglycemic

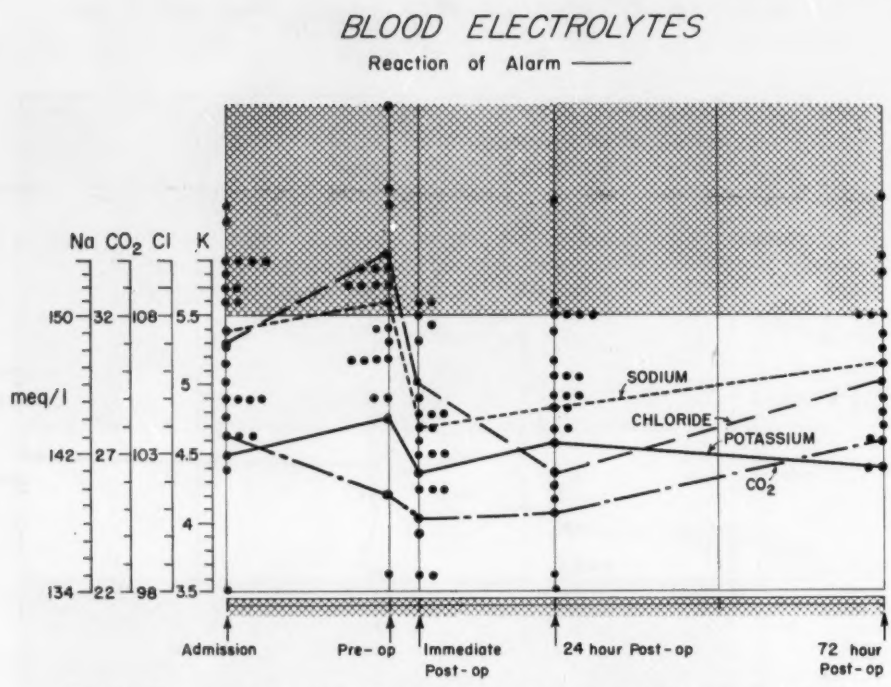


Fig. 2.—The average electrolyte values during the period of surgical alarm are indicated by the line drawings. The change in the values from the fasting determination to the preoperative determination when the intravenous feeding was being given was not significant. The immediate postoperative values showed a consistent, though not statistically significant, change. The individual values were found, on the whole, to be within the normal range as indicated by the unshaded area. The individual determinations for sodium, only, are indicated by the dots.

TABLE 2.—*Blood Sugar and Sulfobromophthalein Determinations*

Fasting		Blood Sugar		
Admission Bl. Sugar, Mg. %	Admission B.S.P., %	Immediate Postop., Mg. %	First Postop. Day, Mg. %	B. S. P. First Postop. Day, %
80	3	210	105	14.5
104	--	443	157	41.0
95	--	224	--	35.0
103	9	265	140	37.0
103	4	245	240	55.0
158	--	257	175	34.0
155	12	318	275	18.0
62	26	242	145	51.0
95	3	220	200	81.5
70	2	275	100	38.0
82	5	225	116	9.7
101		400	150	28.0
Av. 100.7	6.2	277	164	35.9

reactions are not diabetic or latent diabetes because glucose tolerance tests done subsequently were found to be normal.[5]

Blood Urea Nitrogen.—There was a minor but progressive rise in the blood urea nitrogen during the four-day period of parenteral feeding. The rise in the blood urea nitrogen had no detectable relation to the hyperglycemia.

Urine Sugar.—The urine may reveal only a small amount of sugar, usually not commensurate with the degree of hyperglycemia. The urine sugar cannot, therefore, be relied upon as a guide to treatment. Acidosis is not an associated finding of reliable significance.

Clinical Observations During the Hyperglycemic Reaction of Alarm

When the surgical operation has been more extensive, time-consuming, traumatizing, or when the disease process has been extensive, one must keep in mind the possibility of the hyperglycemic reaction of alarm. This reaction usually develops immediately after the operation, although it may develop later in association with other postoperative complications.

The patient is listless, weak, apathetic, and may respond sluggishly to stimuli. He acts a bit drowsy.

The physical examination is noncontributory in establishing a clinical diagnosis. If there is no other associated complication, the vague listlessness of the patient is the most significant warning of this condition. Untreated, the condition may become progressively worse, and the patient may die for no apparent clinical reason.

Our observations have indicated the need for rapid depression of the hyperglycemia in the severe cases by the administration of adequate insulin, lest death supervene. In a few cases the postmortem examination does not reveal a cause for death.

Comments and Conclusions

A hyperglycemic reaction of alarm is a complication which may occur in the postoperative period when the surgical operation is extensive.

Because of the unsuspected nature of this syndrome, the patient's condition may become progressively worse with relatively nonspecific clinical manifestations. Untreated, this reaction of hyperglycemia has been observed to become progressively worse, unto death.

1635 Medical Arts Building (2).

REFERENCES

1. Selye, H.: The Physiology and Pathology of Exposure to Stress, Montreal, Acta, Inc., 1950, p. 117.

2. Erwin, P.; Strickler, J. H., and Rice, C. O.: Use of Polyethylene Tubing in Intravenous Therapy for Surgical Patients, A.M.A. Arch. Surg. 66:673-678 (May) 1953.

3. Rice, C. O., and Strickler, J. H.: Hyperpotassemia and Hyperglycemia: Treatment with Insulin and Invert Sugar, Minnesota Med. 38:565-567 (Aug.) 1955.

4. Rice, C. O., and Strickler, J. H.: Lower Nephron Nephrosis: Function of Kidney When Tubular Degeneration Exists, Am. J. Surg. 90: 347-357 (Oct.) 1955.

5. Rice, C. O., and Strickler, J. H.: Parenteral Nutrition in Surgery, South Dakota J. Med. & Pharm. 9:1-7 (Jan.) 1956.

Surgical Obliteration of a Coronary Artery Fistula to Right Ventricle

HENRY SWAN, M.D.; JOHN N. WILSON, M.D.; GEORGE WOODWARK, M.B., and S. GILBERT BLOUNT Jr., M.D., Denver

Aneurysms of the coronary arteries are not common. Since the first report of surgical correction of an anomalous coronary artery-intracardiac shunt by Björk and Crafoord [1] in 1947, however, the volume of literature dealing with this subject is growing, a manifestation of the increasing interest in the nature of the functional defect produced by these lesions. In a recent editorial, Edwards [2] reviewed the anomalies of the coronary arterial system and a plea was made that such anomalies be classified by functional rather than by older anatomical criteria. It was urged that those anomalies with communications between a coronary artery and a low-pressure cardiac chamber or vessel (an intracardiac arteriovenous shunt) comprise the important group of defects to recognize. These lesions carry a serious threat to the patient's health, yet the majority could be corrected by surgical interruption of the shunt. Steinberg et al.[3] present a comprehensive review of all cases of coronary arteriovenous fistulae reported up to 1958. Emphasis is again placed on recognizing the fact that arteriovenous shunts accompany many coronary artery aneurysms and that the functional defect produced by the fistulae is more important to recognize (and treat) than the more obvious anatomical dilatation of the coronary artery. While we agree with the importance of the functional disturbance, in our opinion, an anatomical classification remains preferable for clarity of description. In this paper, we will use the following terms:

1. Coronary artery aneurysm: an arterial aneurysm without abnormal shunting of blood.

2. Coronary arteriovenous fistula (with or without aneurysm): an arteriovenous shunt through a fistula between a coronary artery and a coronary vein (including the coronary sinus). There may or may not be aneurysmal dilatation at the site of the fistula.

3. Coronary artery-intracardiac fistula (with or without aneurysm): a fistulous communication between a coronary artery and a chamber of the heart: (*a*) right auricle; (*b*) right ventricle; (*c*) left auricle; (*d*) left ventricle.

4. Coronary-pulmonary artery fistula: an anomalous origin of a coronary artery from the pulmonary artery in the absence of transposition of the great vessels.

The abnormal physiology and anatomy will be somewhat different for 3 (*a*) and (*b*), quite different for (*c*), and (*d*) is extremely rare.

Coronary artery-right heart shunts have not been frequently recognized clinically to date, and only a limited number of cases of surgical correction of the defect have been reported. In all of the earlier cases, the true diagnosis was established only after thoracotomy; the preoperative diagnosis was usually patent ductus arteriosus. In February, 1958, Fell et al.[4] reported a group of four cases of congenital coronary artery-intracardiac fistulae in which two of the four cases had been accurately diagnosed prior to surgery. Sanger, et al.[5] also correctly diagnosed this lesion in one of two cases reported. To our knowledge, these are the first three cases of coronary intracardiac shunt previous to that recorded here, which have been recognized preoperatively, confirmed at thoracotomy, and surgically repaired. The diagnosis in these cases was made on the basis of (1) a machinery-like

Submitted for publication April 25, 1959.

From the Departments of Surgery and Medicine of the University of Colorado School of Medicine.

murmur in which the diastolic element was maximal in an abnormal location for patent ductus arteriosus, (2) a left-to-right shunt into the right heart identified by catheterization, and (3) a large tortuous coronary artery shadow on angiocardiogram.

Surgical therapy for this defect has been directed towards interruption of the fistula.[6-10] Simple ligation, and excision and ligation have both been used successfully. With the exception of one case, which was done with a pump oxygenator bypass, all reported cases to date have been corrected without exclusion of the heart from the circulation.

The following case report of a child with a coronary artery-intracardiac fistula with aneurysm represents the fourth such reported case to be properly diagnosed preoperatively and confirmed at thoracotomy. To our knowledge it is the first case to be corrected surgically with the aid of hypothermia and temporary circulatory occlusion.

Report of a Case

The patient (M. F.), a 3-year-old boy, was first seen at Colorado General Hospital in December, 1955. A heart murmur had been noted when the child was 2 or 3 months of age. The child had not had respiratory difficulty, limitation of activity, cyanosis or squatting. The only problem had been frequent upper respiratory infection. Mental and physical development had been entirely satisfactory. Sudden onset of precordial pain or shortness of breath (as is often noted in cases at the time of rupture of a sinus of Valsalva) had not occurred. Physical examination revealed a well-developed and well-nourished white child appearing normal for the stated age of 3 years. Blood pressure was 110/70, pulse 110, respirations 22. The skin was slightly pale. The precordium was prominent and the heart was slightly enlarged to percussion with increased activity. There was a continuous murmur in which the diastolic element was heard best in the fifth interspace at the left sternal border. A Grade II systolic murmur was also heard, maximum in the left second interspace. The second heart sound was widely split with an accentuated pulmonary element. No edema or hepatomegaly was present, and the femoral pulses were easily palpable without noticeable lag.

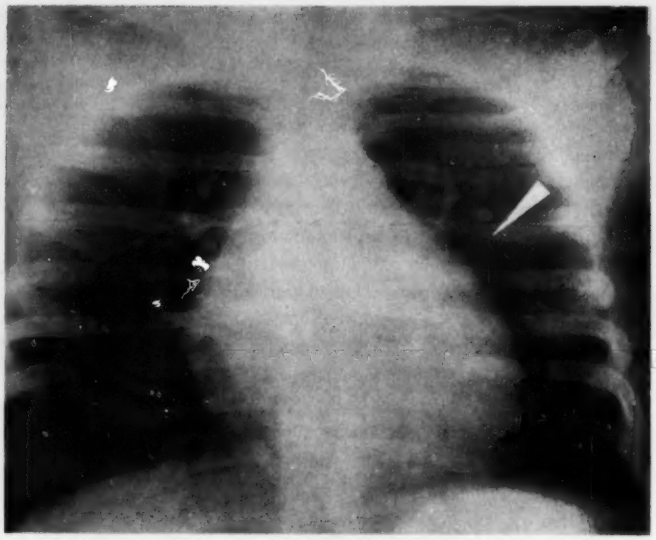
The electrocardiogram revealed left ventricular hypertrophy. Fluoroscopy was interpreted as showing some enlargement of both ventricles, enlargement of the pulmonary artery and its main branches, and increased vascularity peripherally. The blood cell counts and urinalysis were within normal limits. Hemoglobin was 12.4 gm. An atypical ductus or aorticopulmonary window was suspected.

Cardiac catheterization on Dec. 9, 1955, revealed (1) left-to-right shunt at the right ventricular level of approximately 2 vol. %; (2) slightly increased pressure in the right ventricle (35/10), and in the pulmonary artery (34/17). The pulmonary flow was calculated to be 5.1 L/min. while the systemic flow was 3.0 L/min. Thus, there was a left-to-right shunt with increased oxygen saturation in the right ventricle and a pulmonary flow almost twice that of the systemic flow. A retrograde aortogram was done through the left brachial artery and the aorta distal to the left subclavian artery was visualized. No dye went to the lungs. This examination failed to suggest the presence of a patent ductus arteriosus or any other communication between the right ventricle and the aorta distal to the left subclavian artery. The child was discharged on Dec. 13, 1955, with the diagnosis of a communication between the ascending aorta and the right ventricle.

The child was next seen in April, 1957, at which time the boy was still completely asymptomatic. The striking physical finding remained a continuous murmur heard best in the fifth interspace at the left sternal border, notably different from the typical location for a patent ductus or aortopulmonary window, and somewhat low for that arising from a fistula of the sinus of Valsalva into the right ventricle. Fluoroscopy revealed moderate cardiac enlargement and increased pulmonary activity.

In April, 1958, the patient was seen again and had remained free of symptoms. On physical examination, the precordium was somewhat prominent and slightly hyperactive. A continuous "humming" murmur was heard, maximal in the fifth interspace at the left sternal border. Electrocardiogram was interpreted as probable left ventricular hypertrophy. Fluoroscopy revealed normal to slightly increased vascularity of the lungs, left ventricular hypertrophy, and left atrial hypertrophy. The aorta and main pulmonary artery were not remarkable in size or activity. Again, the diagnosis was a fistulous tract between the low ascending aorta and the right ventricle, and this time a coronary artery-right ventricle fistula was considered as the probable diagnosis.

The child was admitted to Colorado General Hospital on Aug. 23, 1958. Preoperative x-rays showed increased vascularity of the lungs. On the left border of the heart, in the region of the left atrial appendage, there was a prominence which appeared abnormal (Fig. 1). No other



1. An anteroposterior roentgenogram of the chest reveals moderate cardiac enlargement. The small bulge along the left contour of the heart was later shown to be caused by the grossly enlarged circumflex artery leading to the fistula.

evidence of left atrial enlargement was noted in other views. Preoperative electrocardiograms showed left ventricular hypertrophy.

On Aug. 25, under general anesthesia, the patient was cooled to 30 C. Exposure was achieved with a bilateral sternal-dividing thoracotomy in the fourth interspace. When the pericordial sac was opened, the moderate enlargement of the left ventricle was apparent. The striking finding on examination of the heart proved to be a gross enlargement of the left coronary artery which was at least 1 cm. in diameter. A normal anterior descending branch, compatible with the size of the heart, was seen to come off of the huge main stem of the left coronary artery. To expose the lesion the heart had to be displaced anteriorly, which required intermittent operation, since the heart did not tolerate this displacement well. The greatly enlarged left coronary vessel continued posteriorly as the left circumflex artery and ended in a 3×1.5×1.5 cm. aneurysmal structure which lay deep in the sulcus just below the coronary sinus and just to the right ventricular side of the interventricular septum (Fig. 2). *A posterior descending branch to the interventricular septum and adjacent portions of both ventricles arose from the enlarged left circumflux artery immediately proximal to the aneurysm.* Palpation over the aneurysm revealed a violent continuous thrill which completely disappeared on occluding the opening

2. With the heart displaced anteriorly, the circumflex artery is seen leading into the aneurysmal dilatation which overlay the large fistula into the upper portion of the posterior aspect of the right ventricle.

between the coronary artery and the right ventricle by invaginating a portion of the aneurysm with the examining finger.

A clamp was placed across the dilated left circumflex artery as close to the aneurysm as possible (but still proximal to the posterior descending artery mentioned above). Immediately, a blue area appeared over the posterior aspect of both ventricles fed by the descending vessel, and the electrocardiogram showed severe changes suggesting myocardial ischemia. As soon as the clamp was removed, the blue area cleared and the electrocardiogram returned to normal.

In order to avoid ligation of this important descending artery to the posterior myocardium, it seemed best to attempt an open, direct-vision, endoaneurysmorrhaphy. With use of total inflow-outflow occlusion, after coronary perfusion with 1.5 cc. of 1:4,000 neostigmine solution, the aneurysm was opened, and the fibrous tissue forming the ventricular orifice was estimated to be about 1 cm. in width and 2.2 cm. in length. Total occlusion time was 5 minutes 45 seconds at 31.5 C, and following restoration of circulation, manual massage and electric shock defibrillation were utilized to achieve an effective heart action. Because a small persistent thrill was present over the aneurysm after the endoaneurysmorrhaphy had been completed, two mattress sutures were placed into the aneurysm so as to fold the crumpled-up sac further into the ventricular orifice of the fistula. This maneuver completely abolished what little thrill had remained after the open procedure. At the close of the operation, the descending artery appeared to be well preserved and the electrocardiogram showed only mild changes of the same type present upon trial clamping of the circumflex artery.

The immediate postoperative course was entirely uneventful. However an electrocardiogram showed that a small acute diaphragmatic myocardial infarction had resulted from the surgical procedure. The child was treated with the usual precautions for infarction with strict bed rest for four weeks. Because of the reduced flow throughout the tremendously dilated coronary artery, as well as the infarct, the patient was started on anticoagulation therapy on the second postoperative day and this was maintained for nearly four weeks. Serial electrocardiograms showed a resolving diaphragmatic infarction during the observation period. The patient was discharged on Sept. 20 to follow progressive ambulation at home. At the time of discharge, as throughout his postoperative observation, auscultation revealed a complete absence of the previous murmur. The child was well and enjoying normal activity when last seen on Jan. 21, 1959, five months after his operation. No murmurs could be heard at this time, and the heart action was quiet.

Comment

In this case, the pathology was a congenital fistula between the left circumflex artery and the right ventricle. The preoperative diagnosis of a fistulous tract between the base of the aorta and the right ventricle was made on the basis of catheterization data showing a left-to-right shunt at the ventricular level and the presence of a continuous murmur over the fifth interspace at the left sternal border, and an unusual cardiac contour on x-ray examination. This localized prominence in the area of the left auricular portion of the left cardiac contour was seen at surgery to be the dilated left circumflex artery seen in contour as it rounded the left border of the heart. This would only occur, we think, when the fistulous tract involves the circumflex artery. In retrospect, we believe this was an important diagnostic sign and when seen should add weight to an already existing suspicion of this diagnosis.

On surgical exposure, the fistulous site was easily located at the point of aneurysmal dilatation near the termination of the left circumflex artery. The extreme dilatation of the entire left circumflex artery proximal to the fistulous connection with the right ventricle with preservation of the normal-sized anterior descending artery will place itself in harmony with the volume of blood flow through it.

Clamping the left circumflex artery proximal to the aneurysm produced gross visual changes and electrocardiographic evidence of severe myocardial ischemia, which quickly reverted to normal upon removal of the clamp. It appeared that ligation of the artery between the posterior descending branch and the fistula was technically impossible because of their proximity and that direct vision endoaneurysmorrhaphy would be essential in order to obliterate the arteriovenous shunt with minimal risk of interrupting myocardial circulation. Fell's opinion that obliteration of the drain-off into the right ventricle may be essential in preventing myocardial

ischemia after division of a coronary artery at some distance proximal to the fistula was not pertinent in this case, as it was clear that the artery could not be ligated at a distance. Hypothermia with inflow and outflow occlusion offered adequate exposure for closure of the large fistula into the right ventricle under direct vision. It is felt that safe obliteration of the arteriovenous shunt could not have been adequately accomplished without direct vision of the fistulous channel entering the ventricle.

Summary

The increasing interest in anomalies of the coronary arteries and in the surgical cure of this disease has led us to submit a revised classification of these lesions.

A case of congenital fistula between the left coronary circumflex artery and the right ventricle is reported.

A prominence in the left cardiac border in the region of the left atrial appendage was present on x-ray. This prominence was caused by the dilated left circumflex coronary artery.

Successful correction of this defect with the aid of hypothermia and direct-vision endoaneurysmorrhaphy was accomplished.

We believe this to be the fourth reported case of this lesion which was correctly diagnosed before surgical exploration and the first case in which this lesion has been corrected under direct vision during hypothermia.

4200 E. 9th Ave. (20).

REFERENCES

1. Björk, G., and Crafoord, C.: Arteriovenous Aneurysm on the Pulmonary Artery Simulating Patent Ductus Arteriosus Botalli, Thorax 2:65, 1947.

2. Edwards, J. E.: Anomalous Coronary Arteries with Special Reference to Arteriovenous-like Communications, Circulation 17:1001, 1958.

3. Steinberg, I.; Baldwin, J. S., and Dotter, C. T.: Coronary Arteriovenous Fistula, Circulation 17:392, 1958.

4. Fell, E. G.; Weinberg, M.; Gordon, A. S.; Gasul, B. M., and Johnson, F. R.: Surgery for Coronary Artery Arteriovenous Fistulae, A.M.A. Arch. Surg. 77:331, 1958.

5. Sanger, P. W.; Taylor, F. H., and Robicsek, F.: The Diagnosis and Treatment of Coronary Arteriovenous Fistula, Surgery 45:344, 1959.

6. Sondergard, T.: Coronary Artery with Aneurysm and Arteriovenous Fistula, in International Symposium on Cardiovascular Surgery, Henry Ford Hospital, Philadelphia, W. B. Saunders Company, 1955, p. 490.

7. Davis, C., Jr.; Dillon, R. F.; Fell, E. H., and Gasul, B. M.: Anomalous Coronary Artery Simulating Patent Ductus Arteriosus, J.A.M.A. 160:1047 (March 24) 1956.

8. Case, R. B., Morrow, A. G.; Stainsby, S. D., and Nester, J. G.: Anomalous Origin of the Left Coronary Artery: The Physiologic Defect and Suggested Surgical Treatment, Circulation 17:1062, 1958.

9. Mozen, H. E.: Congenital Cirsoid Aneurysm of a Coronary Artery with Associated Arterio-Atrial Fistula, Treated by Operation, Ann. Surg. 144:215, 1956.

10. Johnson, J., in discussion of Dr. Fell's paper presented before the International Cardiovascular Society meeting, San Francisco, June 21, 1958.

Intussusception of the Vermiform Appendix Presenting Clinically as a Cecal Carcinoma

JOE CAMPBELL, M.D., and WILLIAM F. McCORMICK, M.D., Memphis, Tenn.

In a recent complete review of the literature by one of us (W. F. M.),[1] intussusception of the appendix was found to have been reported less than 100 times. There were no reports of such an occurrence presenting clinically and radiographically as a cecal carcinoma. This case is presented because of the rarity of the pathological condition and the unusual clinical presentation.

Report of a Case

A 55-year-old Negro woman was admitted to the John Gaston Hospital, a teaching hospital of the University of Tennessee, because of diffuse lower abdominal pain and a right lower quadrant mass.

The patient stated that she had noticed a gradually enlarging abdominal mass for several weeks before coming to the hospital. She described her pain as dull and intermittent in character and aggravated by walking. It was never colicky and did not radiate. She denied melena, nausea, vomiting, diarrhea, and weight loss.

Past history was noncontributory. She had had no previous hospitalization.

Admission examination revealed a well-developed and well-nourished Negro woman in no acute distress. Her temperature was 100.4. F and her blood pressure 137/76. Positive physical findings were limited to the abdomen, where a slightly tender, firm, movable mass measuring approximately 8 cm. in diameter was palpated in the right lower quadrant. No muscle guarding or rebound tenderness was present. Peristalsis was normal. On pelvic examination the above-described mass was palpated in the right adnexal region and could not be separated from the right adnexal structures. Rectal examination was negative. Laboratory findings were within normal limits.

Two barium enemas revealed a large, constant, bosselated filling defect in the medial portion of the cecum. The colon demonstrated no other abnormalities (Figs. 1, 2). The position of the filling defect in the cecum corresponded with the clinically palpable mass. A diagnosis of carcinoma of the cecum was made, and the patient was prepared for bowel surgery.

The abdomen was opened through a right paramedian incision and an 8 cm. mass involving the cecum and terminal ileum was found. There was a marked inflammatory reaction about the mass with adhesions binding it to the right ovary and oviduct. The vermiform appendix could not be visualized. The mesenteric lymph nodes along the ileocolic and right colic arteries were enlarged and firm. No other lesions were visible in the abdominopelvic cavity. A right hemicolectomy with end-to-end ileotransverse colostomy and right salpingo-oophorectomy was carried out.

Her postoperative course was entirely unremarkable, and she was discharged from the hospital on the seventh postoperative day.

Fig. 1.—Barium enema demonstrating bosselated filling defect in cecum.

Submitted for publication May 4, 1959.

From the Department of Surgery and the Department of Pathology, University of Tennessee College of Medicine.

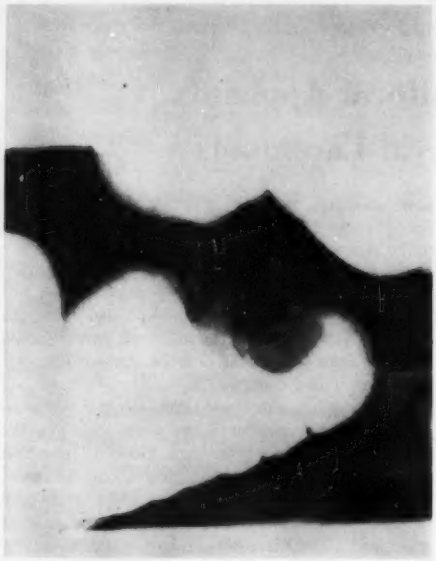


Fig. 2.—Spot film of cecum showing the large filling defect diagnosed clinically as carcinoma.

Pathologic Examination.—The specimen consisted of 18 cm. of cecum and ascending colon, 29 cm. of ileum, a juxtacecal mass, the right oviduct, and right ovary.

The segments of large and small bowel were not remarkable except for mild submucosal edema.

The juxtacecal mass measured 8×6×6 cm. and occupied the position of the vermiform appendix. Fibrous adhesions were present between the mass and ileum, right oviduct, and right ovary. The appendix could not be found prior to dissecting the mass.

When the cecum was opened, a discrete area, 2.5 cm. in diameter and elevated 1 cm. above the cecal floor, was seen. In the center of this roughly conical elevation was a 6 mm. reddish-brown polypoid structure. This lesion corresponded to the area normally occupied by the vermiform appendix.

On dissection of the juxtacecal mass multiple small abscesses filled with yellow pus were encountered. The bulk of the mass was composed of granulation tissue and necrotic omentum. The vermiform appendix, which had intussuscepted into itself, was found in roughly the center of the inflammatory mass. Complete dissection revealed a combination of intussusception Types I and II to be present (Fig. 3).

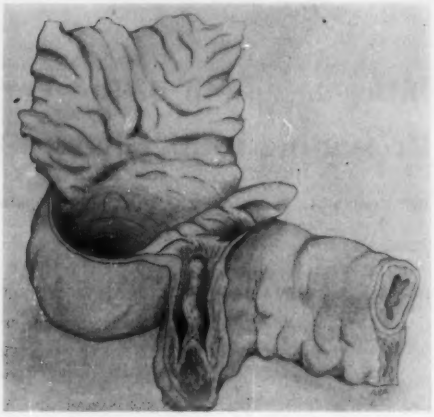


Fig. 3.—Drawing of specimen illustrating the intussusception of the vermiform appendix.

No neoplastic tissue was present in the specimen.

Summary and Conclusion

Intussusception of the appendix is a rare condition, having been reported approximately 100 times in the English-language literature. It is even less common for an appendiceal intussusception to present clinically as a carcinoma of the cecum.

This case is presented as a rare cause of a right lower quadrant mass and a filling defect in the cecum.

Our thanks are extended to Dr. William Dawkins of the Pathology Department for his drawing of the specimen reported here.

858 Madison Ave. (3).

REFERENCE

1. McCormick, W. F.: Intussusception of the Vermiform Appendix with a Mucocele, A.M.A. Arch. Path. 64:686-690 (Dec.) 1957.

Traumatic Pericardial Diaphragmatic Hernia

THOMAS C. MOORE, M.D., Indianapolis

Traumatic diaphragmatic hernia is relatively rare. The defect in the diaphragm may be produced by blunt trauma to the thorax or abdomen or by penetrating gunshot or stab wounds. The herniation generally is into one of the pleural spaces and may lead to pulmonary or gastrointestinal symptoms. The hazard of ischemic gastrointestinal obstruction in these cases has been emphasized by Carter and Guiseppi.[2]

In a few recorded instances, the herniation has occurred into the pericardial sac. The true nature of the pathology in these cases generally has remained obscure prior to operation, and these patients may have been treated for varying periods of time as "cardiac" problems. Only four cases of traumatic pericardial diaphragmatic hernia have been reported. The first of these was described by Crawshaw[3] in 1952. Because of the limited number of recorded cases, it has seemed desirable to report a case of traumatic pericardial diaphragmatic hernia in a 66-year-old woman in whom the symptoms were predominantly of a cardiac nature.

Report of a Case

The patient, a 66-year-old obese white woman, was admitted to the Ball Memorial Hospital on Oct. 10, 1958, for repair of a known left diaphragmatic hernia. Approximately 13 months prior to her admission to the hospital, she had been involved in a serious automobile accident. She had received severe blunt trauma to the left chest and was found to have six fractured ribs on the left side. She experienced dyspnea on admission to the hospital of a neighboring city, and received supportive oxygen therapy during the three weeks she was confined to the hospital after the accident. Symptoms suggesting cardiac disability appeared in the months after her release from the hospital. She experienced shortness of breath and epigastric distress. These were most marked after eating. She vomited occasionally. Tachycardia and periodic episodes of swelling of the extremities also were noted. She was maintained on digitalis for a period of time with relatively little relief of her symptoms. Cardiac consultation was sought by her family physician when she failed to improve. The cardiologist found suggestive evidence of diaphragmatic hernia on cardiac fluoroscopy, and the presence of a portion of the gastrointestinal above the diaphragm was confirmed on roentgen barium examination (Fig. 1). The presence of gas-filled intestine in the area adjacent to the heart was suggested on the roentgenographic examination of the chest (Fig. 2).

On physical examination, the patient was found to be quite obese. She weighed 225 lb. and was 5 ft. 5 in. in height. Her blood pressure was 110/70 mm. Hg and her pulse rate was 88 per minute. No murmurs were heard on auscultation of the heart. Breath sounds were diminished in the lower left chest and peristalsis was heard in this area. The physical examination otherwise was within normal limits. There was no evidence of intestinal obstruction. The electrocardiogram was

Fig. 1.—Roentgenogram following oral administration of barium showing stomach above the diaphragm and in the pericardial sac.

Submitted for publication May 7, 1959.

From the Surgical Service, Ball Memorial Hospital, Muncie, Indiana and the Department of Surgery, Indiana University School of Medicine. Supported in part by a grant from the Indiana Heart Foundation.

Summary of Reported Clinical Experience with

Author	Year	Age	Sex	Nature of Trauma	Associated Injuries	Interval, Traumatic Operation
Crawshaw [2]	1952	48	M	Severe blow to lower right chest		1 year
Stein, Colmore, and Green [3]	1953	45	M	Jeep accident with severe blunt trauma to precordium	Mild concussion; fracture right clavicle	8 years
Brooks [1]	1953	48	M	Knocked down by bus	Fractures of clavicle and ribs	1 year
Smith and Lippert [4]	1958	34	M	Auto accident	Fractures of pelvis; rupture of bladder; severe concussion	7 years
Moore	1959	66	F	Auto accident	Fractures of ribs	1 year

interpreted as showing evidence of digitalis effect. Her red blood cell count was 4,800,000, and her hemoglobin was 13.9 gm. %. The leukocyte count was 10,900. The urine examination was within normal limits, and her serology was negative.

She was taken to the operating room on Oct. 11. Under satisfactory endotracheal anesthesia, her left chest was entered through the bed of the resected eighth rib. Several loops of small intestine were found to have herniated into the left pleural space through a small opening in the diaphragm adjacent to the pericardium. The opening into the pleural space measured approximately 3 cm. in diameter. There was no sac. No adhesions of intrathoracic structures to the herniated loops of small intestine were found. The defect in the diaphragm was enlarged to permit the return of the herniated loops of intestine into the peritoneal cavity. On digital inspection of the extent of the defect, it was found that the greatest portion of the defect communicated with the pericardial cavity. The defect extended across the entire diaphragmatic surface of the pericardium (Fig. 3). Both small intestine and stomach were found in the pericardial cavity. The pericardium was intact except on its diaphragmatic surface. The pericardium was opened, and the viscera which had herniated into the pericardial sac were returned to the peritoneal cavity. The defect in the diaphragm was repaired with interrupted silk sutures, and the pericardium was closed, leaving a small opening to permit the escape of pericardial fluid. The thoracotomy incision was closed in layers, and a

Fig. 2.—Roentgenogram of the chest suggesting the presence of air-filled abdominal viscera within the pericardial sac (arrows).

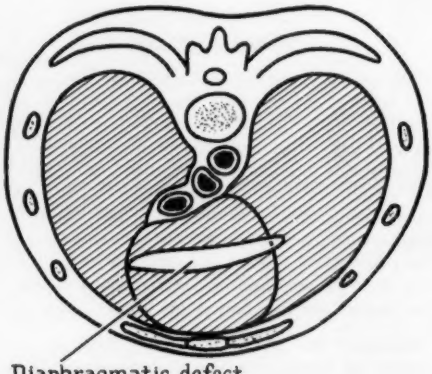


Fig. 3.—Diagram showing the extent of the traumatic pericardial diaphragmatic hernia. The small extension into the left pleural cavity also is indicated.

Traumatic Pericardial Diaphragmatic Hernia

Cardiac Symptoms	Thoracic Cavities Involved in Herniation	Viscera in Pericardial Sac	Operation	Results
Dyspnea and palpitation on exertion	Pericardial only	Stomach; omentum; transverse colon; jejunum	Transthoracic repair	Recovered
Tachycardia, fatigue, and dyspnea on exertion; precordial chest pain, "cardiac" cripple	Pericardial only	Stomach; transverse colon	Transthoracic repair	Recovered
Palpitation and dyspnea with large meal or exercise	Pericardial only	Stomach; omentum	Transthoracic repair	Recovered
None	Pericardial and pleural	Transverse colon; jejunum; left lobe of liver	Transthoracic repair	Recovered
Tachycardia; dyspnea; swelling of extremities	Pericardial largely with small pleural	Stomach; jejunum	Transthoracic repair	Recovered

catheter, which had been left in place during the closure, was aspirated and withdrawn. She tolerated the procedure well and was returned to her room in good condition.

The postoperative course was uneventful and her recovery was prompt. She was released from the hospital 12 days after operation. She has continued to do well since her discharge from the hospital and has experienced complete relief of her preoperative "cardiac symptoms."

Comment

It is apparent from the relief of the patient's cardiac symptoms following repair of the hernia that these symptoms were largely due to the cardiac compression which resulted from the distention of segments of the gastrointestinal tract which were trapped in the pericardial sac. It is of interest that symptoms suggesting heart disease were encountered in four of the five cases recorded in the literature, including the case recorded here (Table). Only the patient described by Smith and Lippert [4] was free of cardiac symptoms. In this patient, the pericardial diaphragmatic defect was associated with a rather sizeable defect into the left pleural cavity. In all of the other recorded cases, the defect was solely or largely into the pericardial sac.

All of the patients were adults, and four of the five were males. All suffered severe blunt trauma to the chest. Fractures were sustained in four of the cases, and in three the fractures involved the thorax. In none of the patients was the diagnosis made or operation carried out in less than a year following the trauma. Intervals of seven and eight years were reported in two cases.

The symptoms were solely or largely cardiac in three cases. Although the patient of Crawshaw experienced dyspnea and palpitation on exertion, vomiting was the symptom which led to his operation. The patient of Smith and Lippert was operated upon because of small bowel obstruction. Transthoracic repair of the pericardial diaphragmatic defect was carried out in all cases and all recovered with relief of symptoms. The pericardial diaphragmatic defects in all but Crawshaw's case were in excess of 3 in. in length. The defect in Crawshaw's case was 1.5 in. in length and with the long axis in the anterior-posterior direction.

Summary

A case of traumatic pericardial diaphragmatic hernia in a 66-year-old woman is reported. Rupture of the diaphragm in the area of the pericardium was sustained as the result of severe blunt trauma to the chest during an auto accident. Multiple rib fractures also occurred. Her symptoms were largely those of heart disease. Successful transthoracic repair of the hernia, with relief of symptoms, was carried out one year after the accident. The literature pertaining to traumatic pericardial diaphragmatic hernia is reviewed.

1100 W. Michigan St.

REFERENCES

1. Brooks, V. S.: Intrapericardial Diaphragmatic Hernia, Brit. J. Surg. 40:511, 1952.

2. Carter, B. N., and Guiseppi, J.: Strangulated Diaphragmatic Hernia, Ann. Surg. 128:210, 1948.

3. Crawshaw, G. R.: Herniation of the Stomach, Transverse Colon and a Portion of the Jejunum into the Pericardium, Brit. J. Surg. 39:364, 1952.

4. Smith, L., and Lippert, K. M.: Peritoneo-Pericardial Diaphragmatic Hernia, Ann. Surg. 148:798, 1958.

5. Stein, J.; Colmore, H. P., and Green, R. A.: Diaphragmatico-Pericardial Tear with Intrapericardial Herniation of the Transverse Colon, Radiology 60:417, 1953.

Reaction of the Colic Mucosa to Surgically Diverted Gastric Juice

An Experimental Study

EDWIN B. MONTENEGRO, M.D.; ALVARO DINO DE ALMEIDA, M.D.; ENIO VITALI, and JOSÉ CARLOS DE ROSA, Sao Paulo, Brazil

Surgery of the esophagus has undergone great improvements in recent years. In most instances today, benign or malignant lesions of the esophagus can be treated surgically. In certain cases, however, when the surgeon must carry out wide resection of this structure to ensure adequate removal of neoplastic tissues, he may encounter great difficulty in restoring physiologic continuity. At other times total cicatricial stenosis may make it impossible to regain physiologic function of the esophagus by any method. On such occasions certain plastic operations devised to produce a neoesophagus offer the surgeon an approach to solution of the problem. If the procedure is successful, the patient can carry on normal oral feeding, since the inconvenience of a permanent gastrostoma is avoided.

Materials employed in plastic surgery of the esophagus have been skin grafts, segments of the gastrointestinal tube, and inert substances, as well as tissues from other organs used in grafting. As a rule, esophagoplasty with skin grafts is restricted to repair of the cervical portion of the esophagus. Segments of stomach and of the large and small intestines, as well as inert substances, are being used with increased frequency in the creation of structures to serve as an esophagus. Construction of substitutes for the esophagus by means of the grafting of tissues, fresh or preserved from other organs, at present is a procedure restricted to experimental surgery, as we [13] demonstrated at the Congress of the American College of Surgeons held in São Paulo in 1953.

Accepted for publication March 7, 1959.

From the Department of Surgical Technique and Experimental Surgery and the Department of Pathological Anatomy of the Faculty of Medicine of the University of São Paulo (Service of Prof. Errico da Silva Bastos).

Previous Studies

Mialaret and associates, in a case of inoperable carcinoma of the esophagus, performed prethoracic esophagoplasty in which the distal end of the large intestine was anastomosed to the posterior face of the stomach. Orsoni and Toupet used the same technique in a case of inoperable carcinoma of the esophagus.

Godard carried out prethoracic esophagoplasty with the right portion of the colon, anastomosing the distal extremity to the stomach, in a patient 7 or 8 years old who had cicatricial stenosis of the esophagus. Lortat-Jacob [8] anastomosed the distal end of the small intestine to the stomach in a case of esophageal stricture caused by caustic agents. Van Prohaska and Sloan also anastomosed the jejunum to the stomach in cases in which they performed prethoracic esophagoplasty with that segment of the small intestine.

Longmire, operating for congenital atresia of the esophagus with hypoplasia of the inferior segment, performed prethoracic esophagoplasty in which the distal end of the jejunum was anastomosed to the stomach. Lafargue and associates considered anastomosis of the colon to the stomach a mistake, since they thought that absence

of a sphincter mechanism would cause distention of the colon with air and regurgitation of the gastric contents when the patient was in the dorsal decubitus position. Furthermore, they wrote, there is the danger of development of a peptic ulcer in the distal part of the colon. Lortat-Jacob,[7] in another case of cicatricial stenosis of the esophagus, accomplished the plastic surgical phase by use of the right portion of the colon and a section of the transverse colon; he anastomosed the distal end of the colon to the jejunum.

Poilleux and Frileux carried out esophagoplasty with the large intestine; they recommended colonojejunal anastomosis to avoid regurgitation of acid from the stomach. Dufour, Lafargue, and Cabanié, in a case of wide resection of the esophagus for a neoplastic lesion, did prethoracic esophagoplasty with the terminal portion of the ileum and the right portion of the colon, anastomosing the distal end of the colon to the second portion of the duodenum. Orsoni and Lemaire, after study of the surgical technique of prethoracic esophagoplasty in which the transverse and descending portions of the colon are used, recommended anastomosis of the distal end of the colon to the jejunum.

Magnant wrote that the segment of large intestine used in plastic surgery of the esophagus can be anastomosed either to the stomach or to the jejunum.

The foregoing studies were not experimental; they concerned clinical observations on patients operated upon. Dragstedt, however, conducted experimental studies in dogs, and observed that if the small intestine or the colon is grafted into the stomach, with adequate preservation of the blood supply, and, if the dogs continue to feed themselves, no lesion of the mucosa will develop. But it was found that when Pavlov's stomach was created and part of the intestine or the colon was implanted therein, the intestinal mucosa was digested.

Sirak and associates implanted portions of the jejunum and colon between the esophagus and the stomach, and reported that no damage to the mucosa of these segments was noted. However, it was found that when histaminic hyperchlorhydria develops erosive lesions will arise in the colic mucosa. Sircus implanted the colon between the gastric antrum and the duodenum in an antiperistaltic position and observed the development of a lesion of the colic mucosa. Mann demonstrated the resistance of the jejunum to the gastric juice and the influence of the adrenal bodies on the formation of the juice.

Skinner and Merendino implanted the jejunum between the esophagus and the stomach and cut the vagus nerves; in another series they carried out gastrectomies in which they extended the resection progressively in each series. After the injection of histamine a lesion of the mucosa of the jejunum was observed if the gastric resection was not sufficiently wide. Kiriluk and Merendino carried out gastrectomy and reconstruction of the transit at the jejunum and ileum. They observed that the more distally the small intestine is placed, the more readily ulceration of the mucosa occurs.

On the basis of the foregoing studies we find no definite guidance on the question of the site of the distal end in anastomotic procedures of the type under consideration. A number of authors prefer the stomach as the site of anastomosis; another group prefer the jejunum as the site of anastomosis, and still another group employs one site on some occasions and another site at other times.

Objective of Study

The purpose of this work was to ascertain how the mucosa of the colon reacts in contact with the gastric juice. This idea arose when one of us (Montenegro) had the opportunity to use the transverse colon to substitute for an esophagus affected by a lye stricture.[12] During the operation some doubt arose as to whether the extermity of the colon should be anastomosed to the stomach or to the jejunum.

We chose to anastomose the colon to the jejunum to prevent regurgitation of acid from the interior of the stomach into the neoesophagus. It is true that exclusion of the stomach from the digestive transit made the operation less physiologic.

In our experimental study we undertook to learn if the mucosa of the colon is or is not damaged by contact with gastric juice, the objective being laboratory evidence for the validity or fallacy of anastomosis of the colon to the stomach.

Material

We employed adult male mongrel dogs. The weight of these animals varied from 8 to 22 kg.

A total of 34 dogs were operated upon. Six animals, however, escaped from the kennel and three others were killed by the management of the Bioterium because of hydrophobia; hence, there remained 25 dogs for study.

Plan

The dogs were divided into two groups. In animals of one group we anastomosed a diverticulum, constructed from a segment of transverse colon, to the gastric antrum. In animals of the second group the same type of anastomosis was made in the gastric fundus.

We proceeded in this manner because it was conjectured that in the antrum the gastric juice would react more intensely on the mucosa of the colon. The final results confirmed this conjecture.

Anesthesia

In every case pentobarbital sodium (Nembutal) was the anesthetic agent. It was dissolved in isotonic solution of sodium chloride in a dose of 0.10 grain for each 3 kg. of body weight. Sometimes it was necessary to complement the anesthesia with the administration of ether. No complications were caused by the anesthesia.

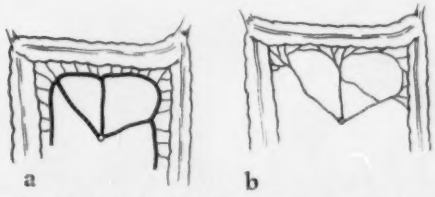


Fig. 1.—(*a*) and (*b*) Two types of vascularization in the large intestine of the dog.

Technical Considerations

A dog was placed in the horizontal dorsal decubitus position. A median abdominal incision about 15 cm. long was employed; it started at the xiphoid process. After the large intestine had been identified, the vascular supply was studied. The vascular supply was of two types.

1. The arterial arcade was somewhat distinct and the vessels were in close apposition to the walls of the colon (Fig. 1*a*). This type of vascular supply was most suitable for isolation and transplantation of a segment of the colon.

2. The arterial arcade was more distinct, with small vessels emerging from it to the walls of the colon (Fig. 1*b*). This type of vascular supply made it difficult to isolate and transplant a segment of colon. In such an instance ligation of the arterial arcade might result in necrosis of the distal portion of colon, as happened with two of our dogs (No. 16 and No. 21). In Dog 16 the necrotic area was resected, and continuity of the large intestine was restored by anastomosis between the transverse colon and the rectum. This dog survived. In Dog 21 the necrotic area was not resected and the dog died of necrosis of the colon, dehiscence of the anastomosis, and peritonitis.

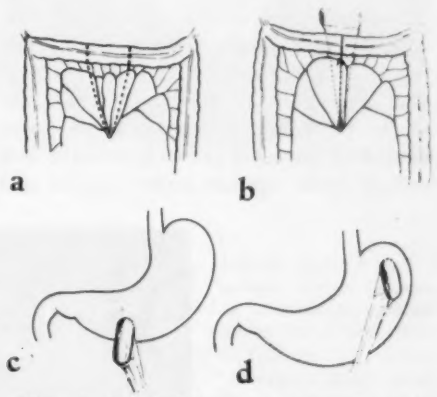


Fig. 2.—(*a*) Isolation of a segment of the transverse colon. (*b*) End-to-end anastomosis of the transverse colon. (*c*) Implantation of the diverticulum in the gastric antrum. (*d*) Implantation of the diverticulum in the gastric fundus.

Fig. 3.—Intact stomach, showing a diverticulum implanted in the frontal aspect of the antrum.

The large intestine of the dog as well as that of man can be divided thus: cecum, ascending colon, transverse colon, descending colon, sigmoid flexure, and rectum.

A segment of intestine about 10 cm. long was isolated at the level of the transverse colon, the vascular supply remaining intact (Fig. 2*a*).

Intestinal continuity was restored by external end-to-end anastomosis of the colon, in two planes, with separate cotton sutures (Fig. 2*b*). The segment of colon thus isolated was anastomosed to the gastric antrum or fundus by terminolateral suture, in two layers, with separate cotton sutures (Fig. 2*c* and *d*). Figure 3 shows a diverticulum implanted in the antrum of the unopened stomach.

The other end of the segment of colon was then closed with cotton sutures and buried in a bag suture. On only one occasion were we unable to accomplish this part of the procedure; at that time we closed the end of the colon in two layers: the first entirely with separate cotton sutures and the second with invaginated Cushing's sutures (No. 30).

In this manner we produced a diverticulum from a portion of the transverse colon and situated it in the gastric antrum or fundus. Figure 4*a* and *b* shows stomachs injected with a contrast medium, with implanted diverticula in the gastric antra or fundi, respectively.

When the diverticulum was implanted in the gastric fundus, the suture line at the level of the anastomosis of course was subjected to tension, as a result of the greater distance between the transverse mesocolon and the gastric fundus. Sometimes, also, tension was produced as a consequence of a shorter vascular pedicle.

In almost all cases the colon-gastric anastomosis involved the proximal end of the colon. Hence, isoperistalsis prevailed. In only two cases was the anastomosis antiperistaltic (Nos. 4 and 5). In both of these cases the segments of colon had been implanted in the gastric antrum, and in one of them a chronic ulcer developed in the diverticulum.

After closure of the gap at the transverse mesocolon and revision of the cavity, the wall was closed in three layers with separate cotton sutures.

Preoperative and Postoperative Data

In the preoperative period the duration of fasting was about 12 hours. In the postoperative period 400,000 units of penicillin was injected every 24 hours for the first two or three days. A liquid diet was employed for 48 hours postoperatively, followed by a normal diet.

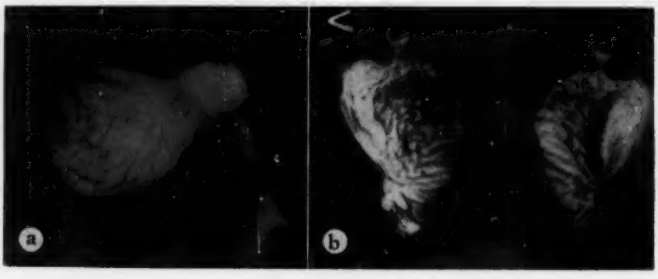


Fig. 4.—(*a*) Stomach injected with contrast medium to show a diverticulum in the gastric antrum. (*b*) Stomach injected with contrast medium to show a diverticulum in the gastric fundus.

Fig. 5.—Intact stomach, showing a diverticulum in the antrum, with a nonspecific, chronic ulcer.

Fig. 6.—The same stomach as shown in Figure 5, in a closer view to show the area of the diverticulum.

Results

First Group. Site of Diverticulum in the Gastric Antrum: Eleven Animals.—Of the 11 animals in this group, two died of wounds caused by fighting with other animals (Nos. 2 and 13) and one died of an unknown cause 24 hours after the operation (No. 5). The other eight animals were killed. The maximal period of postoperative observation in this group was 162 days (No. 1) and the minimal period was 24 hours (No. 5). Except for Dog 5, all the others were observed for 21 days or more before they died or were killed.

In this group necropsy was carried out on 10 dogs. Three nonspecific chronic ulcers were found in the colic diverticulum

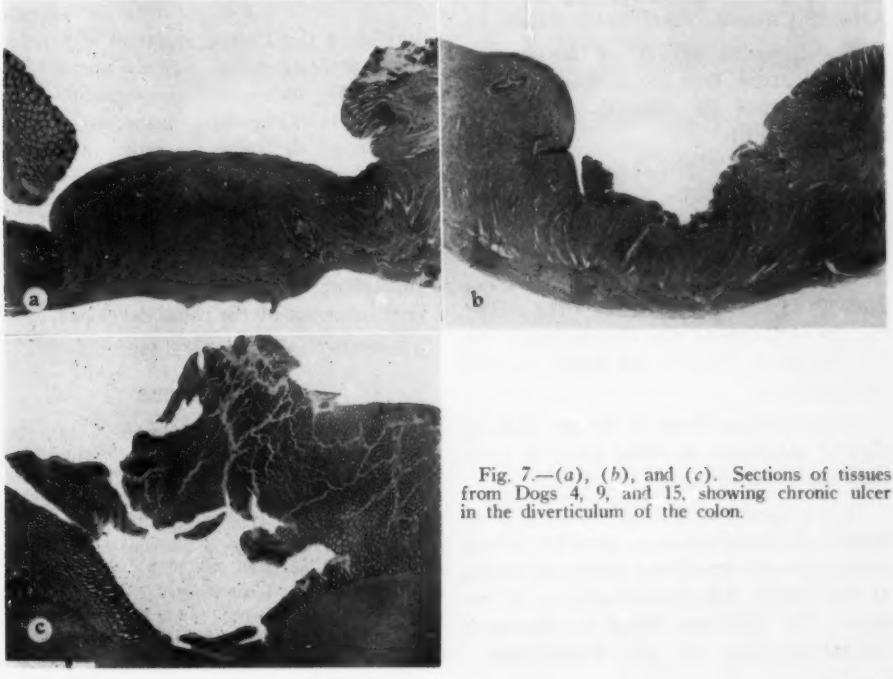


Fig. 7.—(*a*), (*b*), and (*c*). Sections of tissues from Dogs 4, 9, and 15, showing chronic ulcer in the diverticulum of the colon.

(Nos. 4, 9, and 15). In Dog 10 we found eroded areas in the mucosa of the colon.

These gross observations were confirmed by histopathologic examination. Figures 5 and 6 show small and large views of a chronic ulcer localized in the diverticulum. Figure 7*a*, *b*, and *c* are sections of tissue from the chronic ulcers in the colic diverticula of Dogs 4, 9, and 15.

Hence, in the first group of 11 animals, 10 of which came to necropsy, there were three instances of chronic ulcer of the diverticula and one instance of erosion of the mucosa of the colon.

Second Group. Site of Diverticulum in the Gastric Fundus: Fourteen Animals.—Of the 14 animals in this group, 6 died and 8 were killed. Two dogs died of wounds incurred in fighting (Nos. 18 and 29); two died as a result of dehiscence of the colon-colic anastomosis and peritonitis (Nos. 21 and 28); one died after complete dehiscence of the wall (No. 22). In the last-mentioned case we found a foreign body (gauze) in the abdominal cavity. One dog (No. 25) died of purulent peritonitis.

The maximal period of postoperative observation in this group was 117 days (No. 17), and the minimal time was six days (No. 21).

Necropsy was carried out on 13 dogs, and in those instances in which data concerning survival seemed significant, histopathologic examination also was done. These were seven of the latter, as follows: No. 17 (117 days); No. 19 (112 days); No. 20 (110 days); No. 18 (86 days); No. 27 (78 days); No. 31 (44 days), and No. 32 (42 days).

In no case in Group 2 did we find any sign of ulceration, at either gross or histopathologic examination.

In one specimen (No. 27) during histopathologic examination a subacute inflammatory process was found in the submucosa at the gastric side (cicatrization). In another (No. 32), we found an abscess in the submucosa of the colic diverticulum.

Comparative Results.—Among the 10 animals (Group 1) which underwent implantation of the colonic diverticulum in the frontal aspect of the gastric antrum, three instances of chronic ulcer and one of erosion of the mucosa of the colon were observed.

Among the 13 animals necropsied in Group 2 which underwent implantation of the colonic diverticulum in the frontal aspect of the gastric fundus, no instance of acute or chronic ulcer was found.

In view of the foregoing results, we believe that when esophagoplasty is to be performed with use of a portion of the transverse colon, the segment of colon can be anastomosed to the gastric fundus without untoward consequences.

Comment and Summary

We carried out an experimental study in which the reaction of the mucosa of the transverse colon to gastric juice was observed.

Our procedure was to implant a segment of transverse colon, with intact vascular supply, in the frontal aspect of either (1) the gastric antrum or (2) the gastric fundus. We noted the development of a chronic ulcer in three instances, and of erosion of the colonic mucosa in one instance, among animals which underwent implantation of the diverticulum in the gastric antrum. Among the animals which underwent implantation of the colonic diverticulum fundus of the stomach, no lesion in the mucosa of the colon developed.

Rua São Vicente de Paula, 501.

REFERENCES

1. Dragstedt, L. R., and Vaughn, A. M.: Gastric Ulcer Studies, Arch. Surg. 8:791-810 (May) 1924.

2. Dufour, R.; Lafargue, P., and Cabanié, H.: Amputation de l'oesophage thoracique après oesophagoplastie pré-thoracique pour cancer, Presse méd. 60:261-262 (Feb. 20) 1952.

3. Godard, H.: L'oesophagoplastie préthoracique à l'aide du côlon droit (anastomose oeso-caeco-colo-gastrique), Presse méd. 59:314 (March 10) 1951.

4. Kiriluk, L. B., and Merendino, K. A.: The Comparative Sensitivity of the Mucosa of the Various Segments of the Alimentary Tract in the Dog to Acid-Peptic Action, Surgery 35:547-556 (April) 1954.

5. Lafargue, P.; Dufour, R.; Cabanié, H., and Chavannaz, J.: Oesophagoplastie préthoracique à l'aide du côlon droit et de l'iléon terminal, Mém. Acad. chir. 77:362-369 (April 11-18) 1951.

6. Longmire, W. P., Jr.: Antethoracic Jejunal Transplantation for Congenital Esophageal Atresia with Hypoplasia of the Lower Esophageal Segment, Surg. Gynec. & Obst. 93:310-316 (Sept.) 1951.

7. Lortat-Jacob, J.-L.: Oesophagoplastie isopéristaltique transthoraco-médiastinale avec le côlon transverse, Mém. Acad. chir. 77:586 (May 23) 1951.

8. Lortat-Jacob, J.-L.: Un cas d'oesophagoplastie préthoracique du type Blouël, Mém. Acad. chir. 77:672-673 (June 13) 1951.

9. Magnant, M.: A propos des oesophagoplasties préthoraciques avec le côlon droit, Mém. Acad. chir. 77:560-562 (May 23-30) 1951.

10. Mann, F. C.: A Further Study of the Gastric Ulcers Following Adrenalectomy, J. Exper. Med. 24:329-332 (Oct. 1) 1916.

11. Mialaret, M. M. J.; Edelmann, G., and Montagne, J.: Oesophagoplastie, Mém. Acad. chir. 77:343-344 (March 14-April 4) 1951.

12. Montenegro, E. B.; Cutait, D.; Fanganiello, M.; Oliveira, M. R.; Faria, S. G., and Morgante, P. A.: Esofagoplastia transtorácica à custa do côlon transverso, Rev. paulista med. 41:19-23 (July) 1952.

13. Montenegro, E. B.; Vitali, E., and Rosa, J. C.: Emprêgo de segmentos de aorta conservado na cirurgia do esôfago, presented at the Session on Experimental Surgery of the Congress of the American College of Surgeons, São Paulo, Dec. 2, 1953.

14. Orsoni, P., and Lemaire, M.: Technique des oesophagoplasties par le côlon transverse et descendant, J. chir. 67:491-505 (June-July) 1951.

15. Orsoni, P., and Toupet, A.: Utilisation du côlon descendant et de la partie gauche du côlon transverse pour l'oesophagoplastie pré-thoracique, Presse méd. 58:804 (July 8) 1950.

16. Poilleux, F., and Frileux, C.: Deux oesophagoplasties préthoraciques palliatives pour cancer de l'oesophage, Presse méd. 58:1147-1148 (Oct. 18) 1950.

17. Sirak, H. D.; Clatworthy, H. W., Jr., and Elliott, D. W.: An Evaluation of Jejunal and Colic Transplants in Experimental Esophagitis, Surgery 36:399-411 (Sept.) 1954.

18. Sircus, W.: The Resistance to Digestion of the Stomach-Implanted Dog's Colon, Brit. J. Surg. 43:429-435 (Jan.) 1956.

19. Skinner, H. H., and Merendino, K. A.: An Experimental Evaluation of an Interposed Jejunal Segment Between the Esophagus and the Stomach Combined with Upper Gastrectomy in the Prevention of Esophagitis and Jejunitis, Ann. Surg. 141:201-207 (Feb.) 1955.

20. Van Prohaska, J., and Sloan, J.: The Use of the Jejunum in the Construction of an Antethoracic Esophagus, Surgery 22:191-197 (Aug.) 1947.

Unusual Lesions of the Appendix

LIEUT. COL. THOMAS J. WHELAN Jr. (MC), U.S. Army, and CAPT. MAX F. RAST (MC), U.S. Army (Res.)

Introduction

Relatively rare conditions of the appendix are reported as isolated case reports. The finding of three unusual lesions of the appendix during 141 appendectomies, performed at U.S. Army Hospital, Munich, during the 16 months' period from Dec. 29, 1956, through April 30, 1958, is deemed worthy of reporting. The possibility of encountering such lesions at the time of appendectomy must be borne in mind in order that appropriate and adequate surgery be instituted expeditiously.

As can be seen in the Table, 141 appendectomies were performed during this period. Of these, 109 revealed acute appendicitis on histologic examination; 30 showed no significant abnormality, and in 3 unusual lesions were noted. Of these three cases, associated acute appendicitis occurred in two. The unusual lesions which were encountered were (1) a noncaseating florid granulomatous lesion; (2) reticulum-cell sarcoma, and (3) primary adenocarcinoma of the appendix.

Appendectomies, U. S. Army Hospital Munich, Dec. 29, 1956-April 30, 1598

	No. Cases	% Total Cases
Acute appendicitis	109	78
Nonperforated	90	
Perforated	19	
Normal	30 *	21
Granuloma, noncaseating	(1) †	
Reticulum-cell sarcoma	1	0.5
Adenocarcinoma	1	0.5
Total	141	100

* One of these cases showed a microscopic carcinoid.
† This case is included in "acute appendicitis" group.

Submitted for publication May 13, 1959.

From the Surgical Service, U.S. Army Hospital, Munich, Germany.

Report of Cases

CASE 1.—The patient was a 12-year-old white boy, admitted on Dec. 28, 1956, because of lower abdominal pain, anorexia, and fever, present for five hours. At approximately 5 a.m. on the day of admission he had awakened from sleep with pain in the right lower quadrant. There had been no vomiting, and bowel movement had been normal. The past history revealed three things of significance. First, there had been an exposure to tuberculosis in an uncle, who had pulmonary tuberculosis; secondly, he had had a large calcified right hilar node, which had been noted one year previously, and the boy had lived most of his life in the midwestern section of the United States.

Physical examination revealed a slightly obese lad, who did not appear ill. He moved about with no difficulty and ambulated without pain. The temperature was 101 F rectally, the pulse was 86 per minute. Abdominal examination revealed voluntary spasm beneath the right rectus muscle, low in the right lower quadrant, but there was no definite tenderness or mass. Rectal examination was negative initially. The remainder of the examination was normal.

Laboratory studies revealed a total white count of 13,000, with 70% polymorphonuclear leukocytes. Urinalysis was within normal limits.

During the first hospital day symptoms subsided except for fever to 102 F. He was hungry and ate a regular diet without difficulty. However, in the afternoon of the second hospital day, increasing signs of peritoneal irritation in the right lower quadrant, on both abdominal and rectal examination, clearly indicated the necessity of surgical intervention.

Operative Findings.—When the abdomen was opened, clear serous fluid escaped. An absess, walled off by the omentum and ileal mesentery, was found medial to the cecum, with its posterior wall against the posterior parietes. Within the abscess lay a gangrenous perforated appendix. Appendectomy and resection of a portion of the omentum, making up the abscess wall, were performed. The process appeared to be considerably older than the history suggested.

Pathologic Findings.—Acute suppurative appendicitis and periappendicitis were present. In addition, an extensive granulomatous lesion was also noted. There was no caseation within the

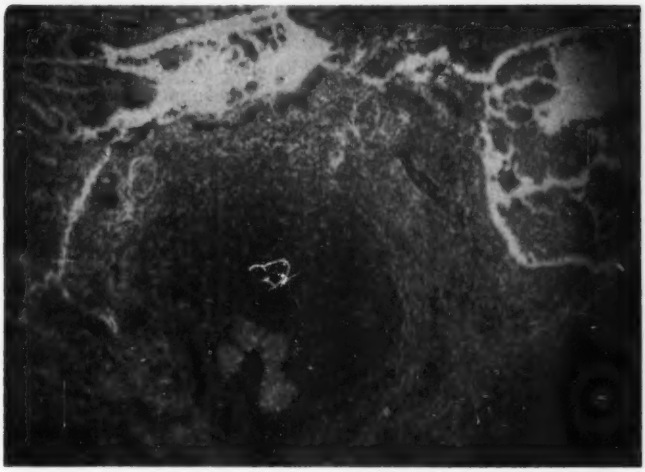


Fig. 1 (Case 1).—Low-power view of sagittal section of the appendix showing granulomata within a submucosal lymphoid follicle (below, center) and appendiceal lumen (above).

granulomata, and acid-fast stains were negative. Granulomata were present in the appendiceal mesentery as well as the appendiceal wall (Figs. 1 and 2). Stains for fungi were performed and were negative. In short, no etiologic agent could be discovered.

Follow-Up.—Although it was felt that his convalescence would be stormy, it was surprisingly without event. He received penicillin, streptomycin, and oxytetracycline for a total of two weeks. He was discharged on Jan. 12, 1957, 14 days postoperatively, on a regular diet, having normal bowel function, and with a healing wound.

The question as to what etiologic agent was responsible for the granulomatous process could not be definitely ascertained. There had been no gross ileocecal disease at operation, although the intense inflammatory reaction, coincident with the perforated appendix, might have obscured intrinsic intestinal disease. Skin tests with PPD and histoplasmin were both 2+. Repeat chest roentgenograms revealed a large calcified right hilar node without active pulmonary disease. No specific therapy for the granulomatous lesion was felt necessary or desirable at that time because the etiologic agent was not known and the patient was asymptomatic and afebrile. The boy was followed in the Surgical Clinic for four months, during which time he did exceedingly well.

The family then rotated to the United States. Shortly after the patient arrived home, the wound, which had apparently been well healed, became acutely inflamed. Because of the history of a granulomatous lesion of the appendix, the patient

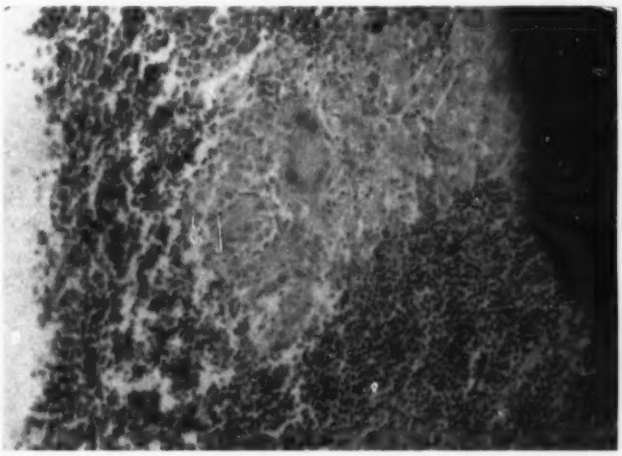


Fig. 2 (Case 1).—Higher-power view of one of the noncaseating granulomata, showing epithelioid cells and one giant cell.

was referred to and hospitalized at Fitzsimmons Army Hospital from May 15, 1957, to June 14, 1957. Here incision and drainage of the wound was necessary, and yielded large amounts of pus. Cultures revealed at first microaerophilic streptococci and later Staphylococcus albus and α-Streptococcus. Rapid secondary healing of the wound then took place. Agglutination studies for brucellosis, typhoid and paratyphoid fever, and tularemia were negative. Hyperglobulinemia and reversal of A/G ratio were present with total protein of 7.7 gm. %, with 2.8 gm. % albumin and 4.9 gm. % globulin. He was discharged without medication, although he had received isoniazid (isonicotinic acid hydrazide), streptomycin, tetracycline, and trisulfapyrimidines (Triple Sulfa) during his hospitalization. His last hospitalization took place at Army and Navy Hospital from Feb. 27, 1958, to March 26, 1958, for repair of an incisional hernia, which was accomplished without event. At this time chest roentgenogram revealed diffuse calcification in the right lung field, as well as the previously noted calcified hilar node.

Comment on Case 1

The case represents a granulomatous and acute suppurative appendicitis with perforation. The exact etiology of the granulomatous lesion is not known. The possibility of histoplasmosis or of sarcoidosis is considered most likely when all factors are taken into account.

In 1950 and 1951 Raftery [14,15] published two reports from the Henry Ford Hospital in Detroit regarding the hitherto unrecognized incidence of histoplasmosis in the appendix and mesenteric lymph nodes. In 2,135 appendix specimens studied, 5% of the slides contained inclusions in the macrophages, identified morphologically by the author as Histoplasma capsulatum. In 43% of the lymph nodes biopsied in cases of mesenteric adenitis in children, similar inclusion bodies were noted. In only one of his "current" cases Histoplasma capsulatum was cultured from the appendix. In four others a pathologic process of lymphoid and reticuloendothelial hyperplasia, similar to the pathologic changes in humans, was produced in mice. Collins [4] has published similar evidence showing an incidence of 7.81% of Histoplasma capsulatum in the appendixes in a total of 50,000 specimens studied. The pathologic changes noted consist either of the "starry sky" phenomenon of reticuloendothelial hyperplasia in the lymph follicles of the appendix or of the mesenteric lymph nodes, with parasite-laden macrophages in the follicles, or a frankly granulomatous lesion, which, on occasion, resembles sarcoidosis. In those granulomata showing no caseation, the organisms are rarely identified. On the other hand, Christopherson et al.[3] believe that the evidence for such a high incidence of a benign form of histoplasmosis in the appendix is far from conclusive and advise more study before such a conclusion be accepted. The majority of reports do not describe a benign form of gastrointestinal histoplasmosis. Rather, they describe associated gastrointestinal lesions only in the fatal disseminated disease.[6,13,18,22]

Although this case must be considered as unproved, there appears to be more indirect evidence supporting the diagnosis of histoplasmosis than that for any other disease.

Case 2.—This 11-year-old white boy was admitted to the U.S. Army Hospital Munich on Sept. 17, 1957, with a 10-day history of periumbilical pain and dysuria. The patient was treated prior to admission with oxytetracycline and penicillin. Because of anorexia, shifting of the pain to the right lower quadrant and temperature elevation to 101 F, the patient was transferred to the hospital.

Physical examination revealed positive findings to be limited to the abdominal and rectal examination. An 8 cm. tense, tender pelvic mass could be felt on rectal examination, and there was poorly localized lower abdominal tenderness on the abdominal examination.

The patient was started on chloramphenicol therapy for two days in an attempt to bring about resolution of the presumed abscess. However, because of continuance of symptoms and impending low small bowel obstruction, extraperitoneal drainage of a pelvic abscess was performed. Ten cubic centimeters of pus and necrotic fibrofatty tissue was obtained. Culture of this material revealed anaerobic streptococci. Biopsy of the abscess wall revealed only acute inflammatory tissue. The postoperative course was uneventful. The patient was discharged on Oct. 7, 1957, on the 20th postoperative day, afebrile and asymptomatic.

The patient was then followed as an outpatient. The pelvic mass remained essentially the same

size. Fever, right lower quadrant cramps, and dysuria recurred and led to his readmission one week later on Oct. 15, 1957.

Physical examination at this time revealed a temperature of 101.6 F, slight right lower quadrant tenderness, suprapubic tenderness, and a hard, tender rectal mass, located in the midline anteriorly. White blood count was 11,000 with a normal differential count.

Appendectomy was performed, since recurrent appendicitis with flare-up of the abscess was thought to be present. A markedly enlarged injected appendix, densely adherent to the area of previous operation and to the pelvic wall was removed. In its greatest diameter at the tip it measured 5 cm. Pathologic diagnosis at this time was old, perforated gangrenous appendicitis, showing chronic, nonspecific inflammatory reaction and periappendiceal abscess. During his hospitalization the mass ulcerated into the rectum, and this area was kept open by repeated digital examinations to allow for proper drainage of the pelvic abscess. It was felt that the residual abscess would subside and that the patient would do well. The patient became afebrile and was discharged after 25 days of hospitalization on Nov. 9, 1957.

Thereafter, his course was unusual in that the pelvic mass grew larger. The patient began to pass blood per rectum. Stools became sparse. Intravenous pyelogram was performed and revealed a blocked hydronephrotic right kidney. Chest x-ray was within normal limits. The patient was readmitted on Nov. 25, 1957, since further surgery was thought to be necessary to alleviate the rectosigmoid obstruction. A soft tissue mass, arising from the pelvis, causing the obstruction, was noted on roentgenogram of the abdomen (Fig. 3). A transverse colostomy was performed on Nov. 29, 1957. The mesocolon was found to be shortened by a mass of matted retroperitoneal lymph nodes, which extended from the pelvis to the mesocolon. Because of this finding the slides of the appendix, removed on Oct. 15, 1957, were reviewed. The appendix and periappendiceal tissues revealed a malignant lymphoma, reticulum-cell sarcoma type (Figs. 4 and 5).

The patient was treated with 10 mg. of mechlorethamine (nitrogen mustard) per day intravenously for a period of four days. White blood count remained between 4,000 and 5,000 per cubic millimeter, with adequate numbers of platelets. Over a three-day period following this treatment, the mass appeared to decrease in size. Thereafter, rapid growth of the mass was noticeable so that it reached almost to the level of the umbilicus in the right lower quadrant.

After 24 days the patient was transferred to the National Cancer Institute, where he received deep irradiation to the abdomen and pelvis. There was some decrease in the large abdominal tumor, but generalized spread of the lymphoma became evident, and he died on Feb. 4, 1958. Autopsy revealed extensive involvement of most body organs with reticulum-cell sarcoma. A large pelvic mass and retroperitoneal masses were present with diffuse involvement of the gastrointestinal tract. Metastases were generalized.

Fig. 3 (Case 2).—Roentgenogram of the abdomen, showing a large soft tissue mass, extending from the pelvis into the right lower quadrant. Impacted feces are noted in the ascending colon with transverse colon distended with gas.

Comment on Case 2

The clinical history and course of the patient presented above is similar in many respects to other reported cases of lymphosarcoma of the appendix. The recognition of the true nature of the disease was delayed, owing to misinterpretation of the tissue submitted for pathologic examination. It is felt that the case was truly of appendiceal origin. The complete replacement of the wall of the appendix with lymphomatous elements in a symmetrical circumferential pattern with no tumor in the base of the appendix speaks in favor of its origin here (Fig. 4). The negative chest x-ray and negative findings elsewhere

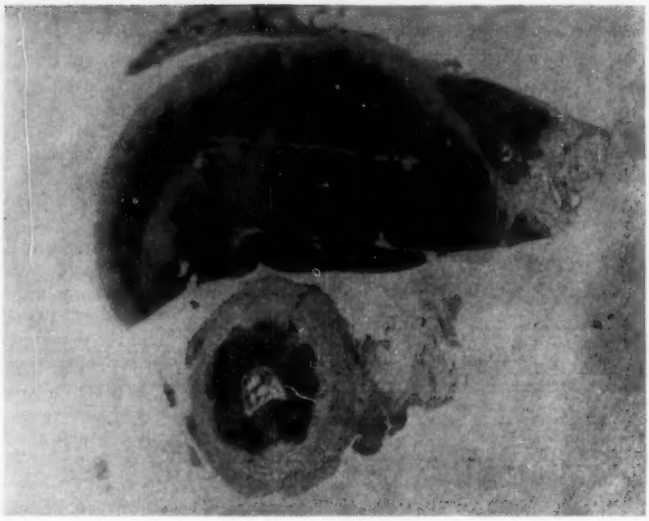


Fig. 4 (Case 2).—Low-power view showing, above, a hemisection of the distal portion of the appendix infiltrated, throughout the submucosa and muscularis, with lymphoma cells. In the upper right corner may be seen lymphomatous involvement of the mesentery. Below is seen the relatively normal base of the appendix with hyperplastic lymph follicles in the submucosa.

in the abdomen during the initial surgery support this view.

Fifty-six cases of sarcoma of the appendix have been reported. Taddei [21] in 1953 reported the most comprehensive review pertaining to this disease, in which he included all of the cases reported by Knox [8] in 1945 and added 24 cases of lymphosarcoma, not previously reported.

The cases reported fall into two distinct clinical patterns. Sarcoma of the appendix presents either as a classical appendicitis or is diagnosed as an incidental finding during laparotomy for an unrelated reason. There is no apparent predilection for age or sex reported. The age range has been from 7 months to the seventh decade of life. The laboratory is of little help in the diagnosis. There is only one case reported in which lymphatic leukemia existed simultaneously with the appendiceal lymphosarcoma.[1] Spreading of disease with an

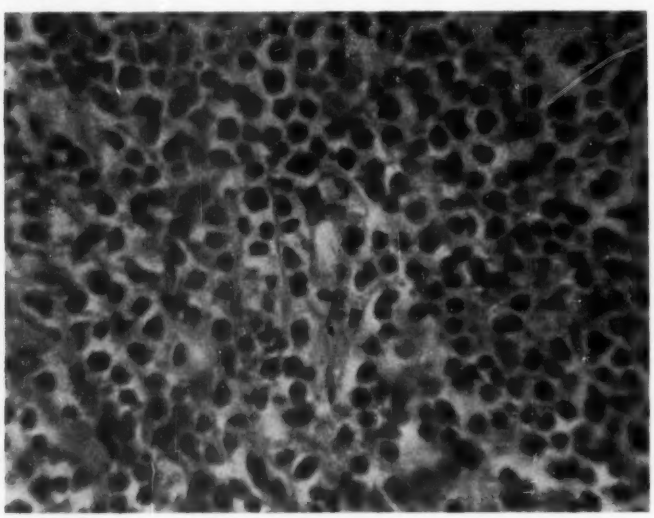


Fig. 5 (Case 2).—High-power view of the lymphoma cells, showing large hyperchromatic nuclei with scant cytoplasm, drawn out into stellate processes in some areas. Uniformity of these large anaplastic cells favors the diagnosis of reticulum-cell sarcoma.

evident abdominal mass precedes the diagnosis by barium enema. Since acute suppurative appendicitis is often coexistent with tumor of the appendix, the recognition of the disease during surgery is often difficult. A mass which is softer than carcinoma, friable and rubbery, and which appears whitish-gray when cut, should lead to the suspicion of lymphosarcoma. Lymph follicles can be seen grossly in giant follicular lymphoma. All histological subgroups of malignant lymphoma have been described, occurring in this location.

Surgical treatment will remain the foremost mode of treatment since the patient usually presents as an acute surgical emergency. Simple appendectomy appears to be as effective as more extensive procedures. Surgery should be followed by irradiation and/or chemotherapy if there is evidence of spread of the disease.

However, no follow-up studies on cases treated other than surgically are available in the literature. The prognosis is guarded. There have been follow-up studies up to four years without apparent recurrence of this disease.[11] The average life expectancy, however, is probably less than one year.[8] Only earlier recognition and prompt institution of accepted therapeutic measures can be expected to improve these figures.

In the case presented, the anaplastic nature of the lesion, plus the fact that when first seen the lesion had extended beyond the organ from which it presumably originated, predisposed toward failure in the arrest of the disease. On the other hand, in the successful cases in the literature, the tumor was limited to the appendix, showing no evidence of spread.

CASE 3.—This 23-year-old white soldier was admitted to the U.S. Army Hospital Munich on Feb. 28, 1958, for an elective interval appendectomy. He gave a history of right lower quadrant pain in October, 1957, and development of a mass in the same area in November, 1957. Barium enema was negative for neoplasm. He was advised to have an elective appendectomy from two to six months later. He was then transferred to Germany in January, 1958. He continued to have a constant vague ache in the right lower quadrant.

Physical Examination.—The patient was a well-developed, well-nourished white man in no distress. He was fully ambulatory. Temperature was 98.4 F; pulse was 76 per minute. The positive findings were confined to the abdomen, where a 4×3 cm. firm, fixed, slightly tender mass was palpated deep in the right lower quadrant. No other masses or organs were palpable. There was no other area of tenderness. Rectal examination was normal.

Laboratory Findings.—Hemoglobin was 15 gm. %; white blood count 10,700 per cubic millimeter, with a normal differential count. Urinalysis was normal.

Course in the Hospital.—On March 3, 1958, laparotomy was performed, at which time a grossly indurated, swollen appendix was dissected with difficulties from the cecum and the ileal mesentery. There was considerable periappendiceal inflammatory reaction. The tip of the appendix was densely adherent to the medial cecal wall; and in removing it, the cecum was opened and was sutured. Because of the degree of reaction and marked induration of the appendix, the specimen was opened in the operating room, and a partially polypoid and partially mucoid infiltrating mass was noted. Frozen section revealed adenocarcinoma of the appendix, and right ileocolectomy and ileotransversocolostomy was performed. There was no evidence of gross metastatic disease in the abdomen. His postoperative course was uneventful, and he was discharged to convalescent leave status on the 14th postoperative day. The patient had a transient bout of partial small bowel obstruction, approximately six weeks after surgery, which responded to conservative measures. When last seen seven months postoperatively there was no evidence of recurrence.

Pathological Findings.—The appendix was 9 cm. in length and varied between 2 and 3 cm. in width. The tumor arose in the middle and distal portions of the appendix, at least 1 cm. away from the base. The tumor was partly papillary (Fig. 6) and partly mucoid, ulcerative, and infiltrating, invading the muscularis (Figs. 7 and 8). All mesenteric lymph nodes were negative for metastases. No other polyps were present in the right colon and in the resected portion of the transverse colon.

General Comment

The statement that adenocarcinoma of the appendix is a low-grade lesion is not substantiated by a review of published reports.[19] This statement has originated because, in the earlier literature, carcinoid or argentaffinoma was called carcinoma

Fig. 6 (Case 3).—Low-power view of the appendix showing transition from normal mucous membrane of the proximal appendix (left) to papillary adenocarcinoma (center and right).

Fig. 7 (Case 3).—Low-power view of another area of the appendiceal carcinoma, where a mucoid, infiltrative growth can be seen invading the muscularis (right).

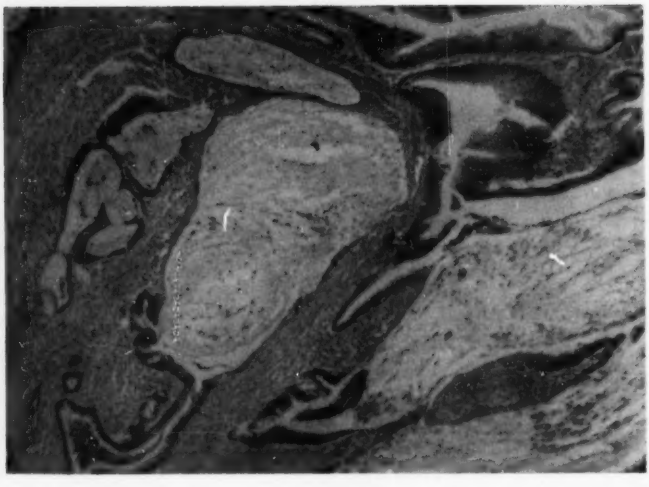


Fig. 8 (Case 3).—High-power view of the adenocarcinoma of the appendix, showing mucous "lakes" lined by neoplastic cells.

Grade I, and obstructive mucocele was likewise considered by some as Grade I carcinoma. Inclusion of these cases in such series would certainly improve prognosis figures. The incidence of this lesion is rare indeed. Collins [4] in 1955 in a study of 50,000 specimens of the human vermiform appendix, found 41 cases of adenocarcinoma (an incidence of 0.082%). This represented both surgical and postmortem specimens. Sieracki and Tesluk [19] reported 8 cases of their own and surveyed the literature to give a total of 50 cases. Raiford [16] stated that the incidence of this lesion was 0.025% of all appendixes examined, while the incidence of all appendiceal tumors was 0.3%. The ratio of carcinoid tumors to adenocarcinoma was 10 to 1. The ages of reported cases ranged from 22 to 82 years with an average age of 55.6 years.

The carcinoma was located in the distal two-thirds of the appendix in 23 cases in which the location was stated and in the proximal one-third in 20 cases. Pathologically, these tumors resemble other large bowel neoplasms. The only correlation between the type of carcinoma and the clinical course was that signet ring adenocarcinoma was rapidly fatal just as it is in large bowel neoplasms. In two-thirds of the cases the patients presented with a clinical picture of acute appendicitis. No preoperative diagnoses have been made. The earliest time at which diagnosis can be expected to be made is at operation, when suspicion of such a lesion prompts performance of frozen section.

The treatment depends upon the degree of invasion. If the mucosa alone is involved or malignant changes noted in the surface of a polyp, appendectomy alone is advised. However, most cases show early involvement of all layers of the appendix; and in these, right ileocolectomy is the treatment of choice. Spread through lymphatics may be early and widespread; therefore, no less extensive resection should be done. Direct peritoneal implantation is common in the fatal cases reported. Blood stream invasion is less frequent than either of the other modes of spread.

In at least 10 cases of the 50 reported by Sieracki and Tesluk [19] death resulted from the lesion. In another eight cases, recurrence of the tumor was demonstrated at later surgery. In their own cases, four of eight patients had died from their appendiceal carcinoma, and four were alive and well between 10 months and 4 years from surgical intervention. It would appear that five-year survival rates would certainly not be better than 50%, and probably considerably lower, although adequate follow-up studies are not available on reported cases.

Summary and Conclusions

Three cases of unusual lesions of the appendix have been presented. These have consisted of (*a*) a granulomatous lesion, possibly histoplasmosis; (*b*) reticulum-cell sarcoma, and (*c*) primary adenocarcinoma.

Coexistence of acute appendicitis complicated two of these cases and in one case caused considerable delay in diagnosis.

The available literature related to each of these conditions has been reviewed.

The importance of suspecting such unusual lesions in cases where the appendix is greatly swollen and indurated and densely adherent to other structures is emphasized. Frozen section histologic study of such suspicious lesions may be of considerable aid in early diagnosis.

2d Field Hospital, APO 407, New York.

REFERENCES

1. Apitz, K., in Festschrift für M. B. Schmidt, Zentralbl. allg. Path. (Supp.) 58:11, 1933.

2. Breuer, M.: Case of Lymphosarcoma of Appendix in Child, Rozhl. chir. 30:568, 1951.

3. Christopherson, W. M.; Miller, M. P., and Kotcher, E.: Examination of Human Appendixes for Histoplasma Capsulatum, J.A.M.A. 149:1648, 1952.

4. Collins, D. C.: A Study of 50,000 Specimens of the Human Vermiform Appendix, Surg. Gynec. & Obst. 101:437, 1955.

5. Henley, F. A., and Slack, W. W.: Lymphosarcoma of the Appendix, Brit. M.J. 1: 378, 1954.

6. Israel, H. L.; DeLamater, E.; Sones, M.; Willis, W. D., and Mirmelstein, A.: Chronic Disseminated Histoplasmosis: An Investigation of Its Relationship to Sarcoidosis, Am. J. Med. 12: 252, 1952.

7. Jason, R. S., and Malloy, H. R.: Giant Follicular Lymphoblastoma of the Appendix, Am. J. Surg. 78:123, 1949.

8. Knox, G.: Lymphosarcoma Primary in the Appendix: A Study of 23 Cases, Arch. Surg. 50: 288, 1945.

9. Maisel, B., and Foot, N. C.: Multiple Polyposis of the Colon with Malignant Change Involving Colon and Appendix, Ann. Surg. 126:262, 1947.

10. Marks, E. S., and Whitaker, H. W., Jr.: Primary Adenocarcinoma of the Appendix, Surgery 27:720, 1950.

11. McSwain, B., and Beal, J. M.: Lymphosarcoma of the Gastrointestinal Tract: Report of 20 Cases, Ann. Surg. 119:108, 1944.

12. Morehead, R. P., and Woodruff, W. E.: Solitary Giant Follicular Lymphoma of the Vermiform Appendix, Arch. Path. 40:51, 1945.

13. Pinkerton, H., and Iverson, L.: Histoplasmosis: 3 Fatal Cases with Disseminated Sarcoid-like Lesions, A.M.A. Arch. Int. Med. 90: 456, 1952.

14. Raftery, A.; Trafas, P. C., and McClure, R. D.: Histoplasmosis: A Common Cause of Appendicitis and Mesenteric Adenitis, Ann. Surg. 132:720, 1950.

15. Raftery, A.: Subclinical Histoplasmosis, J.A.M.A. 145:216, 1951.

16. Raiford, T. S., cited by Sieracki and Tesluk.[19]

17. Rubin, H.; Lehan, P. H., and Furcolow, M. L.: Severe Nonfatal Histoplasmosis, New England J. Med. 257:599, 1957.

18. Shull, H. J.: Human Histoplasmosis: A Disease with Protean Manifestations Often with Digestive System Involvement, Gastroenterology, 25:582, 1953.

19. Sieracki, J. C., and Tesluk, H.: Primary Adenocarcinoma of the Vermiform Appendix, Cancer 9:997, 1956.

20. da Silva, J. N., and Moreira, E.: Linfosarcoma do apêndice (a propósito dum caso), Arq. Pat. (Lisboa), 28:113, 1956.

21. Taddei, G.: Su un caso di reticulo-sarcoma ad Evoluzione linforsarcomatosa della appendice: Contributo casistico e rivista della letterature, Arch. ital. mal. app. diger. 19:497, 1953.

22. Weiss, E. D., and Haskell, B. F.: Anorectal Manifestations of Histoplasmosis, Am. J. Surg. 84:541, 1952.

Segmental Motor Paralysis*

A Cause of Intestinal Obstruction and Ileostomy Dysfunction

THOMAS F. MEANEY, M.D., and CHARLES R. HUGHES, M.D., Cleveland

A mechanical type of intestinal obstruction may result from a localized functional block to peristalsis. This interruption of peristaltic activity in a segment of intestine is usually secondary to a variety of abdominal diseases. This concept of functional block or "segmental motor paralysis" is applied to a group of patients with clinical and radiological manifestations of a mechanical type of intestinal obstruction but in whom no anatomical block of the lumen was encountered at surgery. A segmental motor paralysis is also believed to be the underlying cause of ileostomy dysfunction in a certain group of patients with infection of the ileostomy stoma. Examples of this type of intestinal obstruction are presented with further explanation as to the probable mechanism causing this functional obstruction.

Panel I.—The first panel simply reviews the usual types of intestinal obstruction, with particular emphasis upon three points. Two radiographs and a drawing are shown to represent first an adynamic ileus, in which there is generalized dilatation of the intestine and no specific point of mechanical obstruction; the radiographs illustrate this type of dilatation. The two clinical points which are emphasized in adynamic ileus are (1) the lack of peristalsis or hypoperistalsis and (2) the absence of crampy abdominal pain.

Submitted for publication April 28, 1959.

* Surgery illustrated. Shown as a scientific exhibit of the Section on Radiology at the 107th Annual Meeting of the American Medical Association, San Francisco, June 23-27, 1958.

From the Department of Radiology, The Cleveland Clinic Foundation and The Frank E. Bunts Educational Institute. Present address of Dr. Meaney is 10515 Carnegie Avenue (6).

Next are presented the radiographs from a case of mechanical intestinal obstruction, with a drawing to illustrate the localized mechanical block of the lumen. It is emphasized that the clinical distinctions of hyperperistalsis and crampy abdominal pain are important in this type of obstruction. These distinctions will be used in the next panel to differentiate this type of obstruction from segmental motor paralysis.

Panel II.—This second panel is designed to explain the nature of segmental motor paralysis. The concept of segmental motor paralysis as a cause of intestinal obstruction is illustrated by a drawing showing an inflamed area of ileum which has produced an obstruction. The line drawing which accompanies this panel is intended to demonstrate the fact that in segmental motor paralysis there are the following features:

1. A patent intestinal lumen.
2. Hyperactive peristalsis in an attempt to bypass the area involved.
3. The fact that the patient experiences a crampy abdominal pain as seen in a true mechanical intestinal obstruction. The reason for the obstruction lies in the fact that the segment of intestine is not able to transmit the peristaltic wave, and hence a mechanical type of obstruction results despite the fact that the lumen is patent. The panel lists some of the causes of this type of obstruction.

Panel III.—This panel contains radiographs from several cases of segmental motor paralysis resulting in intestinal obstruction. In all of these cases, the patient experienced clinical signs of mechanical obstruction. On physical examination the patient exhibited hyperperistaltic activity, but, to differentiate this entity from a mechanical obstruction, none of these patients had any

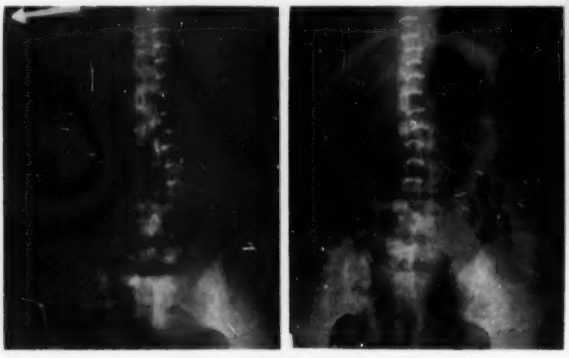
physical occlusion of the lumen of the intestine. Rather, the obstruction was caused by a localized inflammatory involvement of a segment of intestine, usually secondary to inflammatory disease outside of the intestine itself.

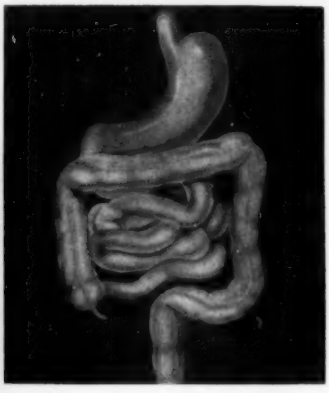
Panel IV.—This panel demonstrates how the concept of segmental motor paralysis applies to many cases, if not the majority of cases, of ileostomy dysfunction, which occur in the absence of a recurrent disease. By diagram, this panel shows a finger inserted into an ileostomy, demonstrating no occlusion of the lumen. The radiographs show that barium can be instilled into the distal portion of the ileum without evidence of ob-

Panel I: Intestinal Obstruction

Adynamic (Paralytic) Ileus

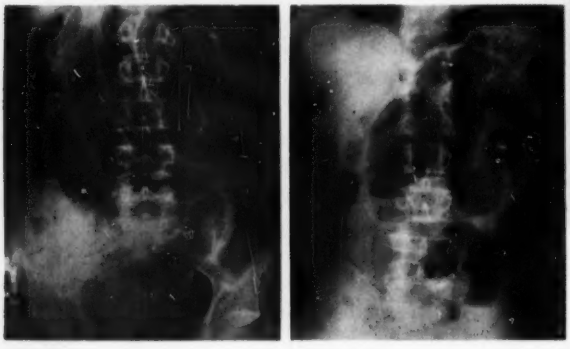
Peristalsis: absent or ineffectual
Gas Pattern: generalized dilatation
Nature of Obstruction: generalized absent or ineffectual peristalsis





Mechanical Obstruction

Peristalsis: hyperactive initially
Gas Pattern: dilatation proximal to obstruction
Nature of Obstruction: physical agent occludes lumen



struction. Yet, the patients demonstrate a clinical and radiographic type of mechanical intestinal obstruction, despite the fact that no block of the lumen is present. Most of these patients were operated on, and at operation the most consistent feature was inflammation of the ileostomy stoma either on the skin or just below in the abdomen. It is believed that this obstruction results from the inability of this inflamed segment of ileum to transmit the peristaltic wave.

Panel II: Segmental Motor Paralysis

Peristalsis: hyperactive

Gas Pattern: dilatation proximal to obstruction

Nature of Obstruction: localized segment with absent or ineffectual peristalsis

Causes of Segmental Motor Paralysis

Localized Inflammation
- Appendiceal Abscess
- Pelvic Inflammatory Disease
- Diverticulitis
- Regional Enteritis
- Ileostomy Dysfunction

Neurologic Disease
- Hirschsprung's Disease

Miscellaneous
- Lupus Erythematosus

Panel III: Examples

Pelvic peritonitis

Pelvic peritonitis

Perforated regional enteritis

Appendiceal abscess

Pancreatic fistula

Lupus erythematosus

Panel IV: Segmental Motor Paralysis

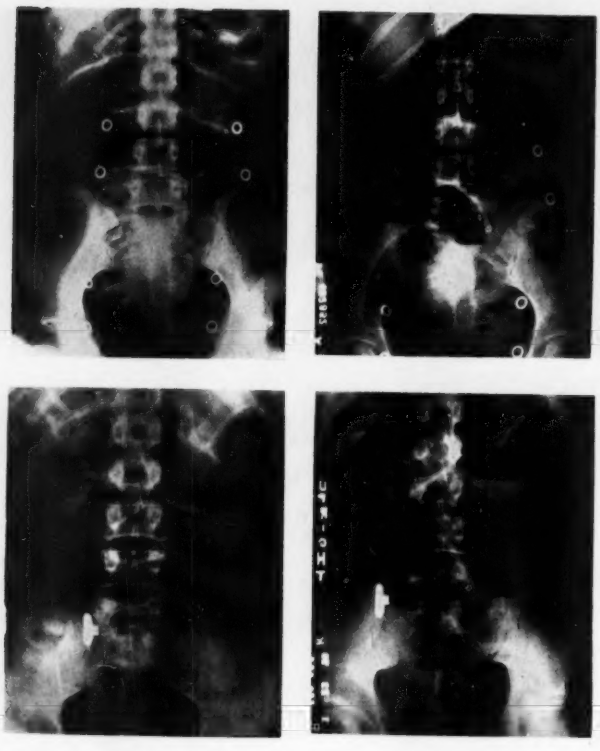
Segmental Motor Paralysis is the Common Cause of Ileostomy Dysfunction

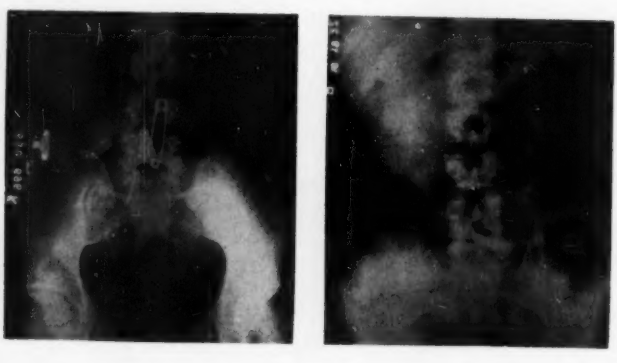
Patent Lumen

Free Passage of Contrast Material

Clinical Signs of Mechanical (Complete, Partial) Obstruction

Roentgen Findings of Intestinal Obstruction





Pictorial Film Reviews

Cholecystectomy and Operative Cholangiography

JOEL W. BAKER, M.D., and JOHN H. WALKER, M.D., Seattle

This motion picture illustrates the technical points that have been adopted by us in developing practical operative cholangiography in conjunction with cholecystectomy. Close cooperation of the radiologist and the surgeon in an endeavor to eliminate all possible sources of error attains a greater degree of accuracy in diagnosis of common duct stones than surgical exploration or palpation alone. When this procedure is performed carefully and interpreted with the accumulated experience of past performance, it is dependable, frequently obviating common duct exploration in otherwise doubtful cases. The dependability will vary with the interest and ability of the professional team, the availability of equipment, and the frequency with which operative cholangiography is practiced. The surgical technique of cholecystectomy is well demonstrated in the film. The indications and judgment in three different circumstances are emphasized.

Received for publication April 23, 1959.

Department of Surgery (Dr. Baker) and Department of Radiology (Dr. Walker), The Mason Clinic.

Motion picture presented at the 107th Annual Meeting of the American Medical Association, San Francisco, June 25, 1958.

Fig. 1.—Dr. Joel W. Baker, the co-author and operating surgeon in this film, is Chief of Surgery, Virginia Mason Hospital and the Mason Clinic. He discusses indications for operative cholangiography, noting that 20% of all gallbladder stones have associated common duct stones.

Fig. 2.—The presence of common duct stones cannot be predicted with complete accuracy on the basis of history and laboratory studies alone. Small stones in the cholecystogram point toward increased probability of encountering common duct stones. Layered stones in decubitus position.

Fig. 3.—The technician is placing the bantam movable grid apparatus on the operating table. One is routinely placed under the patient at every cholecystectomy, whether cholangiography is contemplated or not.

Fig. 4.—For anesthesia giving best relaxation and long duration, intercostal deep splanchnic block is recommended. Under thiopental (Pentothal) sedation tetracaine (Pontocaine) is injected subcostally into each intercostal nerve, T-5 through T-12 bilaterally. The celiac plexus is then blocked paravertebrally at T-12.

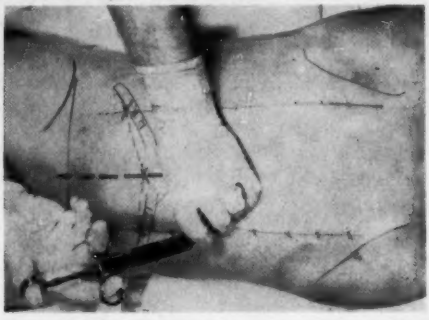


Fig. 5.—Before the patient is draped, a control film is taken to check position of biliary tract over the cassette and to arrive at an optimum technique. The long cylinder produces better quality radiographs and lends protection to personnel.

Fig. 6.—After technician directs positioning, the patient is not moved. Rotation of patient is not necessary. Long timer switch cord allows technician to stand at distance at time of exposure. Equipment is 100 ma. rotating anode 100 kvp; 2 mm. aluminum filter added.

Fig. 7.—The film is developed and technique adjusted if necessary. The cassette is reloaded in readiness for operation. A marker on the floor may be useful in recentering the machine after its removal.

Fig. 8.—In case at hand, because of small size of stones in gallbladder and because of frequent attacks of colic, the common duct is under suspicion. The cystic duct is isolated.

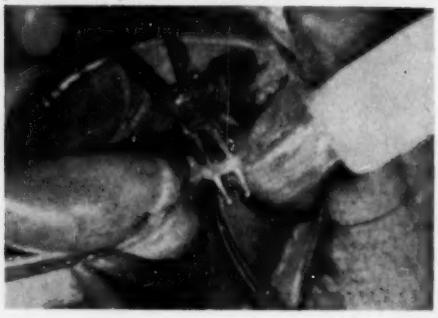


Fig. 9.—In preparation for cholangiogram, the cystic duct is tied. The suture is retained as a future anchor to the tube to be inserted. Against the steadying index finger the cystic duct is cut halfway across.

Fig. 10.—A long polyethylene tube of small caliber is inserted by way of the cystic duct into the common duct. It is marked to avoid inserting beyond the common duct into the duodenum. The tube is first filled completely with saline to eliminate air bubbles.

Fig. 11.—This tube is then anchored to the first suture, and a second suture is tied below to make it watertight and stable.

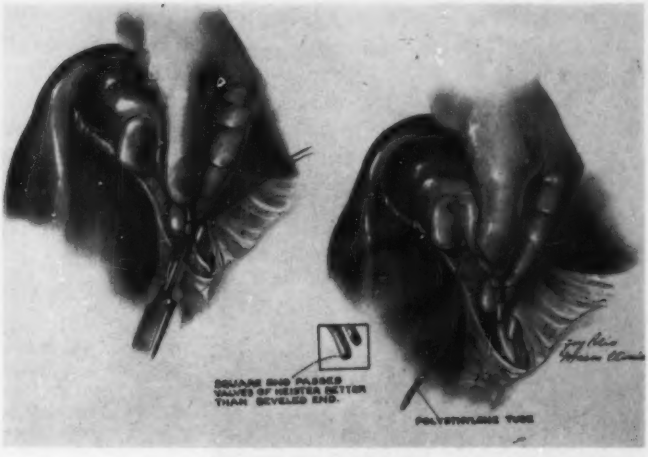


Fig. 12.—Before x-ray, all instruments, sponges, and surgical pads are eliminated from the field. The point where the common duct dips behind the duodenum is marked by the crease in the overlying towel. The radiographic tube is then centered on this crease.

Fig. 13.—From 4 to 6 cc. of 35% iodopyracet (Diodrast) is injected slowly. When injection is complete the anesthetist arrests respiration and signals the technician. Exposure time is never over 0.3 second. Kilovoltage and focal film distance are variables. Fast screens are used.

Fig. 14.—A second cassette is inserted and the procedure repeated immediately. One film frequently confirms or clarifies findings of the other. A stereoscopic pair may be taken if desired. Solutions in adjacent darkroom are maintained at 75 F, reducing processing time to three minutes.

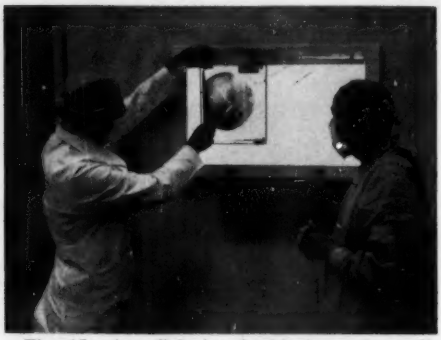


Fig. 15.—A radiologist should always be available to consult with the surgeon concerning interpretation of the cholangiogram. He is alerted at time film is taken to avoid delay.

Fig. 16.—Note two small stones in distal common duct. Either or both could be missed on exploration. Knowing the number of stones in advance of exploration saves time and undue morbidity of unnecessary manipulation.

Fig. 17.—The tube is removed and the cystic duct divided. A less encumbered field is secured by first removing the gallbladder. The stones are removed by scoop in right hand from opposite side of table.

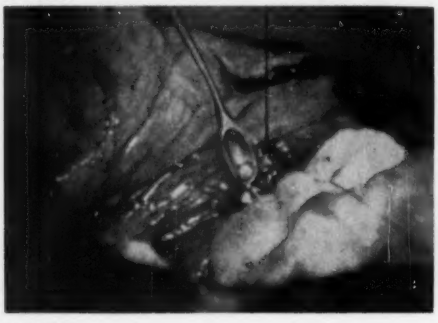


Fig. 18.—To avoid overlooked stones, the cholangiogram is repeated. By temporary insertion of a polyethylene tube into the T-tube, air may be flushed from it. Reflux into pancreatic duct may be from excessive pressure employing too large a volume.

Operative Cholangiography

DEWARD O. FERRIS, M.D., and JOHN R. HODGSON, M.D., Rochester, Minn.

Cholecystectomy is a satisfactory operation for the diseased gallbladder which contains stones; the operation is followed by unsatisfactory results in only 5% to 10% of cases. Yet this small percentage of unsatisfactory results is somewhat misleading, since, when the tremendous number of such operations performed is considered, the actual number of unsatisfactory results becomes a problem of considerable magnitude. The use of operative cholangiography is one means of lessening the number of unsatisfactory results.

This film illustrates in detail the technique of operative cholangiography and also shows the techniques of cholecystectomy, choledocholithotomy, and choledochostomy. The teamwork involved in the actual taking of the radiographs is shown. Technically satisfactory results can be obtained with mobile x-ray equipment, with the use of a Lysholm grid as a secondary diaphragm. The contrast medium is a 35% solution of iodopyracet (Diodrast). Two cases are used to demonstrate fully all phases of the technique. A method of avoiding air bubbles in the cholangiogram taken after exploration of the common bile duct is demonstrated. Radiographs from several cases demonstrate the usefulness of the procedure.

Received for publication April 28, 1959.

Section of Surgery (Dr. Ferris) and Section of Roentgenology (Dr. Hodgson), Mayo Clinic and Mayo Foundation.

Motion picture presented at the 107th Annual Meeting of the American Medical Association, San Francisco, June 25, 1958.

Fig. 1.—A portion of the table pad is removed from the operating table to accommodate a transverse aluminum tunnel, which affords a means of introducing and removing the cassette.

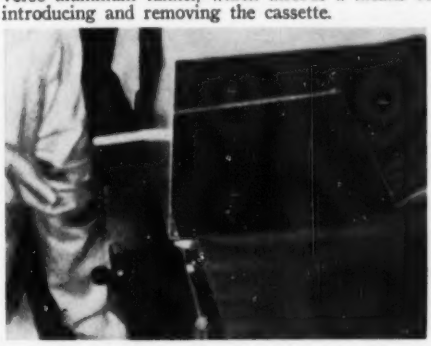


Fig. 2.—The patient is positioned on the table in proper relationship to the cassette. The thickness of the body overlying the tunnel is accurately measured.

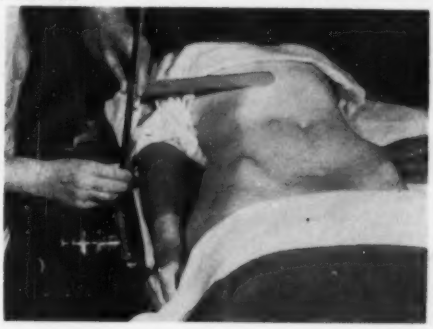


Fig. 3.—The surgeon then proceeds with the usual exposure of the gallbladder and bile ducts. Wound towels are fixed in place with absorbable surgical sutures (catgut) rather than with metal clips.

Fig. 4.—A ligature is placed at the upper end of the cystic duct. A small Polythene tube is introduced into the distal part of the cystic duct, advanced into the common bile duct, and fixed by a ligature. This tube is then filled with bile by simple aspiration.

Fig. 5.—All radiopaque objects are removed, and the cassette is introduced. To assist in filling the biliary tree, the patient is placed in the Trendelenburg position. A 25-degree right-lateral tilt places the position of the common bile duct so that it will be free of the vertebral column in the roentgenogram.

Fig. 6.—The anesthesiologist produces a state of apnea; the x-ray tube is brought into position; 2 to 5 cc. of iodopyracet is injected, and the first exposure is taken.

Fig. 7.—While the cassette is being changed, the lateral tilt is eliminated; an additional 10 to 15 cc. of the contrast medium is injected, and the second exposure is made.

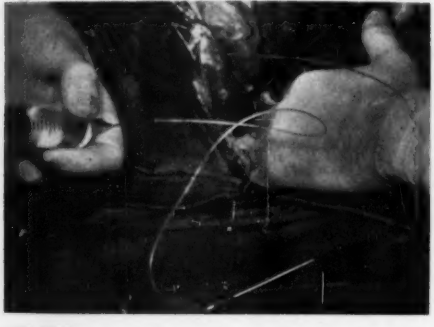


Fig. 8.—While the cholangiograms are being developed, the surgeon usually proceeds with cholecystectomy.

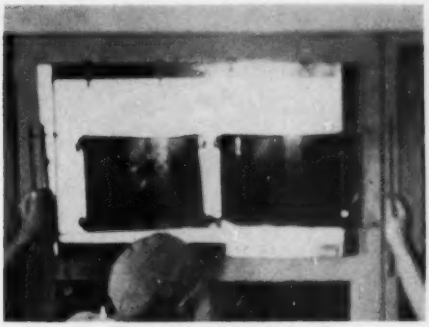


Fig. 9.—The processed cholangiograms are brought to the operating room for examination. The information gained is added to that already at hand, and a decision is made regarding further surgery.

Fig. 10.—In this particular case the condition disclosed by the cholangiogram is entirely normal.

Fig. 11.—This cholangiogram depicts an unsuspected stone in the lower end of the common bile duct.

Fig. 12.—The stone is being removed. After choledocholithotomy we always insert a T-tube. The technique of secondary cholangiography is similar to that of primary cholangiography, except that the medium is now injected through the T-tube.

Fig. 13.—To exclude air bubbles, the patient is placed in the Trendelenburg position and the T-tube is connected to an intravenous set. While isotonic saline solution is run in, the duct is gently manipulated to dislodge air bubbles and to cause them to float up into the duodenum.

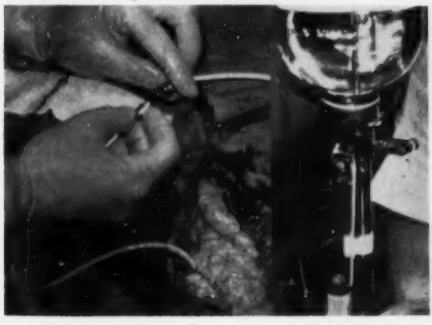


Fig. 14.—The secondary cholangiogram now shows a normal biliary tree; no stones remain, and the medium freely enters the duodenum.

Fig. 15.—The cholangiogram in another case reveals that a long segment of cystic duct has been overlooked.

Fig. 16.—In another instance, the cholangiogram reveals a slightly dilated common bile duct, but the medium in the duodenum depicts a filling defect which proves to be a carcinoma of the ampulla of Vater.

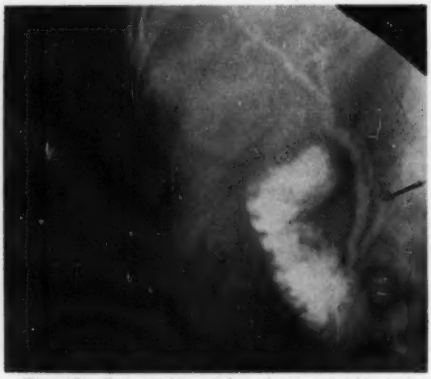


Fig. 17.—Interesting and perhaps valuable information is demonstrated in this cholangiogram, which shows that the medium passes easily from the common bile duct into the pancreatic duct.

Fig. 18.—In cases of suspected stones of the common bile duct cholangiography is helpful in determining the number and location of such stones, well illustrated in this cholangiogram.

PROVEN EFFECTIVE FOR THE TENSE AND NERVOUS PATIENT

"There is perhaps no other drug introduced in recent years which has had such a broad spectrum of clinical application as has meprobamate.* As a tranquilizer, without an autonomic component in its action, and with a minimum of side effects, meprobamate has met a clinical need in anxiety states and many organic diseases with a tension component."

Krantz, J. C., Jr.: The restless patient—A psychologic and pharmacologic viewpoint. Current M. Digest 25:68, Feb. 1958.

Miltown®

the original meprobamate, discovered and introduced by

WALLACE LABORATORIES, *New Brunswick, N. J.*

CM-215

LEDERLE INTRODUCES...

a masterpiece

greater antibiotic activity

Milligram for Milligram, DECLOMYCIN exhibits 2 to 4 times the activity of tetracycline against susceptible organisms. (*Activity* level is the basis of comparison—not quantitative blood levels—since action upon pathogens is the ultimate value.*) Provides significantly higher serum activity level . . .

with far less antibiotic intake

DECLOMYCIN demonstrates the highest ratio of prolonged activity level to daily milligram intake of any known broad-spectrum antibiotic. Reduction of antibiotic intake reduces likelihood of adverse effect on intestinal mucosa or interaction with contents.

unrelenting peak antimicrobial attack

The DECLOMYCIN high activity level is uniquely constant throughout therapy. Eliminates peak-and-valley fluctuation, favoring continuous suppression. Achieved through remarkably greater stability in body fluids, resistance to degradation and a low rate of renal clearance.

*Hirsch, H. A., and Finland, M.: *New England J. Med.* 260:1099 (May 28) 1959.

DECLO

Demethylchlortetracycline Lederle

# of antibiotic design

plus
"extra-day"
activity

FOR PROTECTION AGAINST RELAPSE

DECLOMYCIN maintains activity for one to two days after discontinuance of dosage. Features unusual security against resurgence of primary infection or secondary bacterial invasion—two factors often resembling a "resistance problem"—enhancing the traditional advantages of tetracycline... for greater physician-patient benefit

in the distinctive, dry-filled, duotone capsule

immediately available as:
DECLOMYCIN
Capsules, 150 mg.,
bottles of 16 and 100.
Adult dosage: 1 capsule
four times daily.

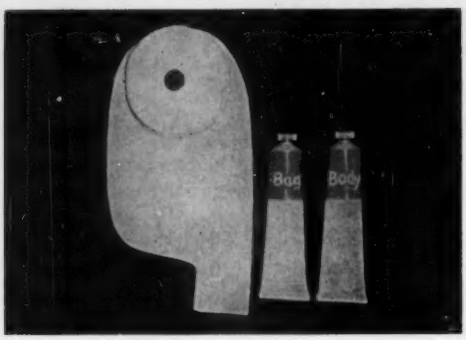
MYCIN®

Lederle

LEDERLE LABORATORIES
a Division of
AMERICAN CYANAMID COMPANY
Pearl River, New York

CUSTOM MADE

RUBBER ILLEOSTOMY COLOSTOMY APPLIANCES



- CHEMICALLY TREATED TO HELP ELIMINATE ODOR.
- CEMENTED TO BODY WITH OUR SPECIAL ADHESIVE CEMENT.

For information write to:

GERARD PRODUCTS

Dept. A

7875 Oakleaf Ave., Elmwood Park, Chicago 35, Ill

Here are several booklets on mental hygiene that may prove of interest and use to you and your patients.

EMOTIONAL HEALTH IN WORK AND PLAY
T. R. Retlaw, 8 pages, 15 cents

HYPNOTISM—HUMBUG OR HEALING
James A. Brussel, 6 pages, 10 cents

YOUR STAKE IN MENTAL HEALTH
George S. Stevenson, 4 pages, 10 cents

THE PSYCHIATRIST Edward Dengrove and Doris Kulman, 6 pages, 10 cents

BOOKLETS ON MENTAL HYGIENE

Keep a supply of these booklets on hand. Available at lower cost for quantity purchases.

AMERICAN MEDICAL ASSOCIATION
535 North Dearborn Street • Chicago 10 • Illinois

Of interest to you and your patients

THE MENACE OF ALLERGIES

FOOD ALLERGY
by Samuel M. Feinberg, M.D., 6 pages, 10 cents

SKIN ALLERGY
by Samuel M. Feinberg, M.D., 6 pages, 10 cents

ASTHMA AND HAY FEVER
by Samuel M. Feinberg, M.D., 6 pages, 10 cents

AMERICAN MEDICAL ASSOCIATION
535 NORTH DEARBORN STREET • CHICAGO 10 • ILLINOIS

For the first time

CONVENIENCE and ECONOMY

for that all-important first dose of broad-spectrum antibiotic therapy

New

TERRAMYCIN®

brand of oxytetracycline

INTRAMUSCULAR SOLUTION

Initiation of therapy in *minutes after diagnosis* with new, ready-to-inject Terramycin Intramuscular Solution provides maximum, sustained absorption of potent broad-spectrum activity.

...and for continued, compatible, coordinated therapy

COSA-TERRAMYCIN®

oxytetracycline with glucosamine

CAPSULES

Continuation with oral Cosa-Terramycin every six hours will provide highly effective antibacterial serum and tissue levels for prompt infection control.

The unsurpassed record of clinical effectiveness and safety established for Terramycin is your guide to successful antibiotic therapy.

Supply:

*Terramycin Intramuscular Solution**
100 mg./2 cc. ampules
250 mg./2 cc. ampules

Cosa-Terramycin Capsules
125 mg. and 250 mg.

Cosa-Terramycin is also available as:
Cosa-Terramycin Oral Suspension — peach flavored, 125 mg./5 cc., 2 oz. bottle
Cosa-Terramycin Pediatric Drops — peach flavored, 5 mg./drop (100 mg./cc.), 10 cc. bottle with plastic calibrated dropper

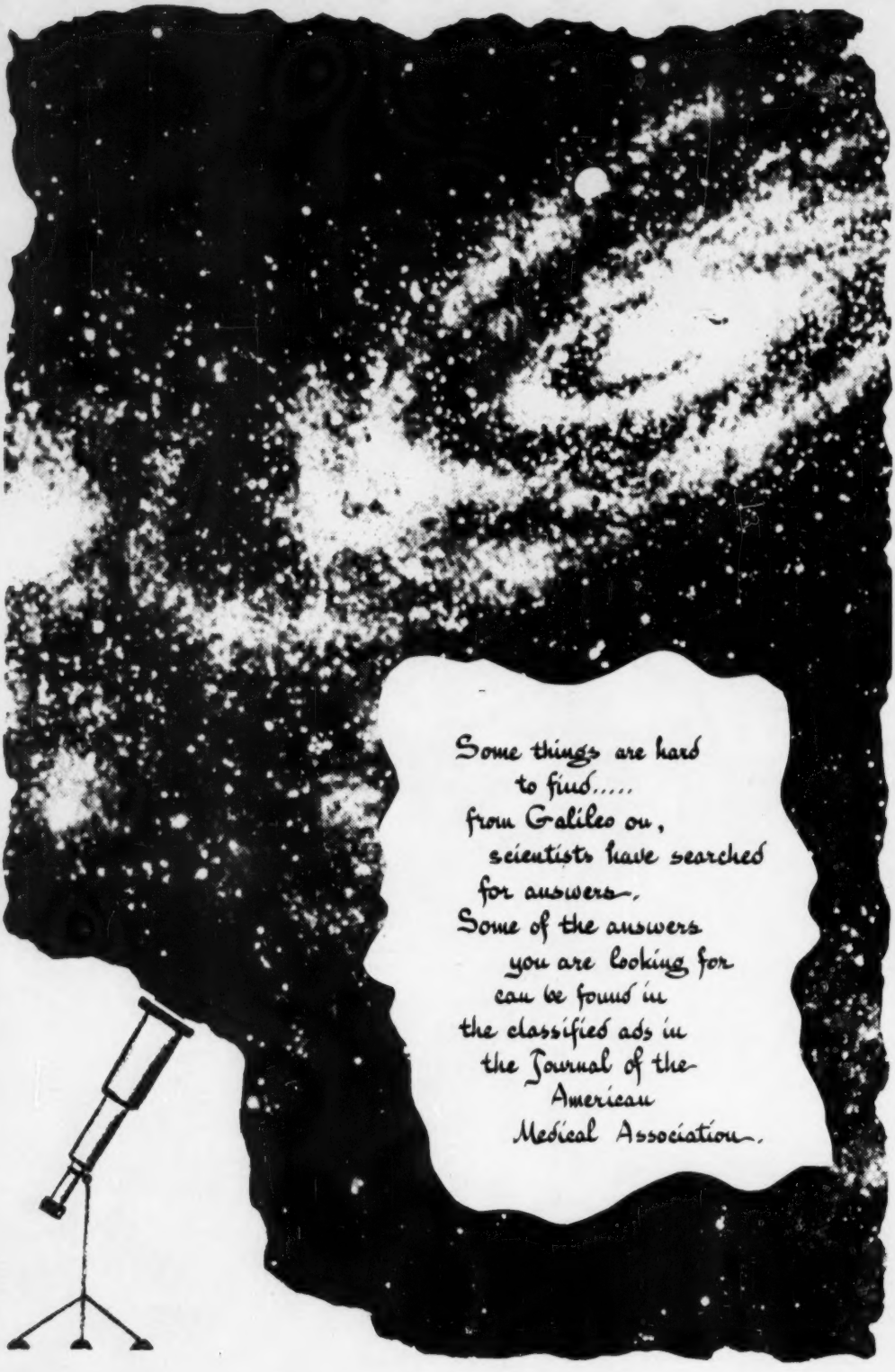
Complete information on Terramycin Intramuscular Solution and Cosa-Terramycin oral forms is available through your Pfizer Representative or the Medical Department, Pfizer Laboratories.

*Contains 2% Xylocaine® (lidocaine), trademark of Astra Pharmaceutical Products, Inc.

Pfizer

Science for the world's well-being™

PFIZER LABORATORIES, Division, Chas. Pfizer & Co., Inc., Brooklyn 6, N.Y.


Some things are hard
to find.....
from Galileo on,
scientists have searched
for answers.
Some of the answers
you are looking for
can be found in
the classified ads in
the Journal of the
American
Medical Association.

Show it LIFE-SIZE for reality . . .

EXPLORATORY FENESTRATION of left humerus with partial removal by curettement of lesion in marrow cavity. Incision at anterolateral aspect of arm near insertion of deltoid muscle.

Show it with the Kodak Cavalcade Projector, Model 510

Here is a projector that does the slide changing for you —automatically—at preselected intervals. Also, you have your choice of three semiautomatic methods of slide changing. And, by flipping a switch, you select 300- or 500-watt illumination. Superb Kodak Ektanar Lens for brilliant, sharp pictures! Auxiliary lenses available.

For scientific exhibits, choose the Kodak Cavalcade Repeating Projector, Model 540; it projects a series of slides over and over again, automatically.

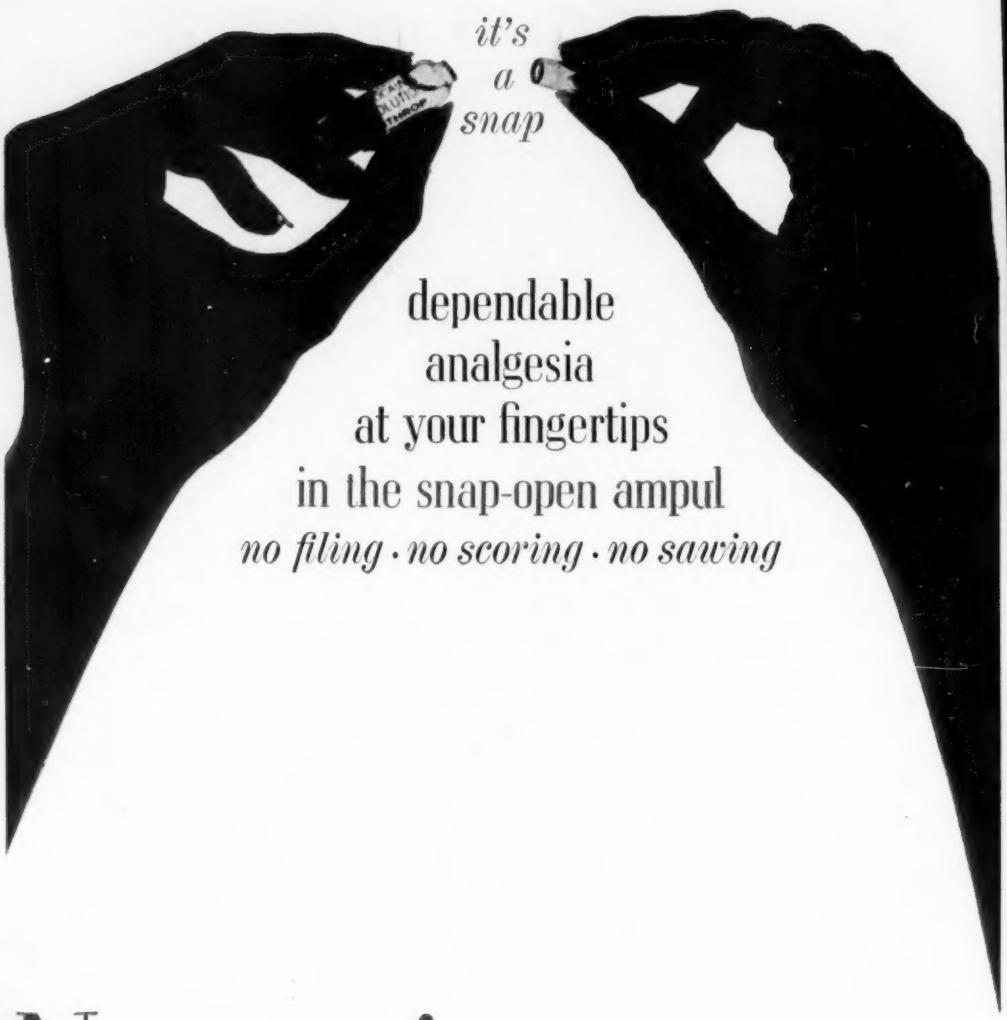
Prices—the de luxe Kodak Cavalcade Projector, Model 510, $159.50; Model 520, $124.50; Model 540, $199.50. *(Prices are list and subject to change without notice.)* For details, see your Kodak photographic dealer or write:

40 cardboard slides can be placed in No. 1 metal tray (included with projector). No. 2 tray holds 30 glass, metal, cardboard or plastic slides.

EASTMAN KODAK COMPANY, *Medical Division*, Rochester 4, N. Y.

Serving medical progress through Photography and Radiography

Kodak
TRADE MARK



dependable
analgesia
at your fingertips
in the snap-open ampul

no filing · no scoring · no sawing

Novocain®

PIONEER BRAND OF PROCAINE HYDROCHLORIDE

a local anesthetic with universal acceptance

Novocain 1%, 2%, 10%, 20% Solutions with or without vasoconstrictors.
Also available: Multiple Dose Vials with dual purpose caps for withdrawal by needle or pouring.

Winthrop LABORATORIES, NEW YORK 18, N. Y.